

=> fil reg

FILE 'REGISTRY' ENTERED AT 17:48:04 ON 11 MAR 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 MAR 2003 HIGHEST RN 497818-02-7

DICTIONARY FILE UPDATES: 10 MAR 2003 HIGHEST RN 497818-02-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que 129

```
L1          STR
      8      10
      O      G1
      /      /
G2 ^Cb--S--N--N--C--G3
 1  2  3  4  5  6  7
      /      /
      O      9
```

VAR G1=O/S

VAR G2=S/C/N/O

VAR G3=C/N

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L3 1570 SEA FILE=REGISTRY SSS FUL L1

```
L23          STR
      8      10
      O      G1
      || 3   ||
G2--Cb--S--N--N--C--G3
 1  2  3  4  5  6  7
      || 3   ||
      O      9
```

VAR G1=O/S

VAR G2=S/C/N/O

VAR G3=C/N

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

RECEIVED  
MAR 11 2003  
CAS REGISTRY  
STN 1570

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

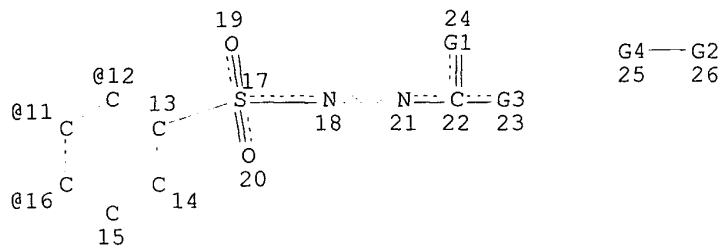
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L25 1534 SEA FILE=REGISTRY SUB=L3 SSS FUL L23

L27 1461 SEA FILE=REGISTRY ABB=ON PLU=ON L25 AND 46.150.18/RID

L28 STR



VAR G1=O/S

VAR G2=S/C/N/O

VAR G3=C/N

VAR G4=12/11/16

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 11

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L29 1435 SEA FILE=REGISTRY SUB=L27 SSS FUL L28

100.0% PROCESSED 1461 ITERATIONS

1435 ANSWERS

SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 17:28:39 ON 11 MAR 2003)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 17:28:49 ON 11 MAR 2003

L1 STR  
L2 50 S L1  
L3 1570 S L1 FUL  
SAV L3 GERSTL994/A

FILE 'HCAPLUS' ENTERED AT 17:30:23 ON 11 MAR 2003

L4 512 S L3  
E HAMILTON G/AU  
L5 64 S E3,E17,E18  
E HAMILTON GREG/AU  
L6 133 S E3-E6,E9,E10  
E BELYAKOV S/AU  
L7 153 S E3-E14  
E VAAL M/AU  
L8 26 S E4,E5,E8,E9

L9           E WEI L/AU  
           271 S E3-E18  
           E WEI LING/AU  
 L10          86 S E3-E11  
 L11          24 S E12-E22  
           E WU Y/AU  
 L12          629 S E3,E25  
           E WU YONG/AU  
 L13          150 S E3,E33  
 L14          5 S E97  
           E STEINER J/AU  
 L15          63 S E3,E13  
 L16          3 S E42  
 L17          112 S E61,E63,E64  
           E GUILFORD/PA,CS  
           E GUILF/PA,CS  
 L18          419 S E5-E24  
 L19          200 S E25-E40  
 L20          416 S GUILFORD?/PA,CS  
 L21          1 S L4 AND L5-L20

FILE 'REGISTRY' ENTERED AT 17:34:25 ON 11 MAR 2003

L22          1 S 433977-26-5  
 L23          STR L1  
 L24          50 S L23 SAM SUB=L3  
 L25          1534 S L23 FUL SUB=L3  
           SAV L25 GERSTL994A/A  
 L26          36 S L3 NOT L25  
 L27          1461 S L25 AND 46.150.18/RID  
 L28          STR L23  
 L29          1435 S L28 FUL SUB=L27  
           SAV L29 GERSTL994B/A

FILE 'HCAPLUS' ENTERED AT 17:42:56 ON 11 MAR 2003

L30          1 S L22  
 L31          451 S L29  
 L32          5987 S CYCLOPHILIN? OR CYP OR IMMUNOPHILIN?  
 L33          1 S L31 AND L32  
 L34          25 S L31 (L) THU/RL  
 L35          55 S L31 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX  
 L36          193 S L31 AND P/DT  
 L37          24 S L36 AND L34,L35  
 L38          24 S L21,L30,L33,L37  
 L39          7 S L34 NOT L38  
 L40          1 S L39 AND ?MALAR?  
 L41          25 S L38,L40  
 L42          30 S L35 NOT L37-L41  
 L43          13 S L42 AND BENZ?/SC,SX  
 L44          9 S L41 AND BENZ?/SC,SX  
 L45          22 S L43,L44  
 L46          16 S L41 NOT L45  
           SEL DN AN 10 15 16  
 L47          3 S E1-E9 AND L46  
 L48          25 S L45,L47

FILE 'REGISTRY' ENTERED AT 17:48:04 ON 11 MAR 2003

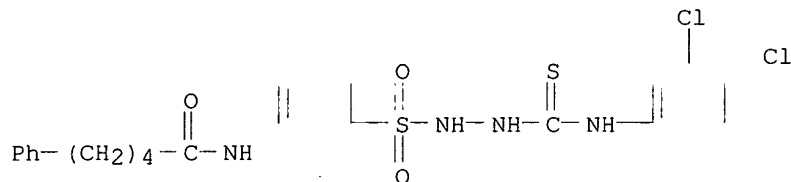
=> d ide can l22

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 433977-26-5 REGISTRY

CN Benzenesulfonic acid, 3-[(1-oxo-5-phenylpentyl)amino]-,  
 2-[[[(3,4-dichlorophenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX

NAME)  
 FS 3D CONCORD  
 MF C24 H24 Cl2 N4 O3 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:20228

=> fil hcaplus  
 FILE 'HCAPLUS' ENTERED AT 17:48:21 ON 11 MAR 2003  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 11 Mar 2003 VOL 138 ISS 11  
 FILE LAST UPDATED: 10 Mar 2003 (20030310/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 148 all fhitrstr tot

L48 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2002:588980 HCAPLUS  
 DN 137:135080  
 TI Modification of NSAIDs by sulfur-containing functional groups  
 IN Lai, Ching-San; Wang, Tingmin  
 PA Medinox, Inc., USA  
 SO U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 602,688.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-48  
 ICS A61K031-405; A61K031-255; A61K031-40; A61K037-34

NCL 514411000

CC 1-7 (Pharmacology)

Section cross-reference(s): 25, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6429223	B1	20020806	US 2000-715767	20001117
	US 6355666	B1	20020312	US 2000-602688	20000623
	WO 2002000167	A2	20020103	WO 2001-US19750	20010619
	WO 2002000167	A3	20020404		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	AU 2001070010	A5	20020108	AU 2001-70010	20010619
PRAI	US 2000-602688	A2	20000623		
	US 2000-715767	A1	20001117		
	WO 2001-US19750	W	20010619		
AB	A method for the alleviation of side effects induced by the administration of a nonsteroidal anti-inflammatory drug (NSAID) to a subject comprises chem. modifying the NSAID by covalent attachment of a sulfur-contg. functional group, such as sulfoxide, sulfonate, reverse sulfonate, sulfonamide, reverse sulfonamide, sulfone, sulfinatate, or reverse sulfinatate to provide prodrugs. The max. blood concn. (Cmax) of the prodrug is reduced relative to the unmodified NSAID by about 10-90%. For example, oral administration of a naproxen prodrug, i.e., a conjugate of naproxen and tosylate (prepn. given), resulted in the release of free naproxen. In rats, the prodrug had equiv. pharmacol. efficacy and greatly improved gastrointestinal safety profile compared to naproxen.				
ST	nonsteroidal antiinflammatory prodrug sulfur functional group side effect				
IT	AIDS (disease) (AIDS dementia complex; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Mental disorder (AIDS dementia; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Nervous system (Huntington's chorea; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Arthritis (adjuvant; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Respiratory distress syndrome (adult; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Transplant rejection (allotransplant; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Nervous system (amyotrophic lateral sclerosis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Heart, disease (angina pectoris; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Artery (angioplasty, postangioplasty; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)				
IT	Nervous system				

- (central, trauma; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Fatigue, biological  
(chronic fatigue syndrome; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Pain  
(chronic; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Artery, disease  
(coronary; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Nervous system  
(degeneration, chronic; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Mental disorder  
(depression; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Penis  
(disease, priapism; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Gastrointestinal motility  
(disorder, dysmotility; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Heart, disease  
Kidney, disease  
(failure; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Stomach, disease  
(gastritis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Kidney, disease  
(glomerulonephritis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Transplant and Transplantation  
(graft-vs.-host reaction; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Neoplasm  
(hematol.; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Dialysis  
(hemodialysis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Shock (circulatory collapse)  
(hemorrhagic; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Functional groups  
(hydrocarbyl; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Appetite  
(hyperphagia; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Intestine, disease  
(ileitis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Lymphocytic choriomeningitis virus  
(infection; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Intestine, disease  
(inflammatory; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)
- IT Head  
Lung, disease  
Reperfusion

(injury; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Brain, disease  
(ischemia; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Headache  
(migraine; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Myeloproliferative disorders  
(myelofibrosis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Heart, disease  
(myocarditis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Anti-inflammatory agents  
(nonsteroidal; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Pancreas, disease  
(pancreatitis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Peritoneum  
(peritonitis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT Ovarian cycle  
(premenstrual syndrome; prodrugs of NSAIDs contg. sulfur-contg. functional groups for alleviation of side effects during therapy)

IT AIDS (disease)

Alzheimer's disease

Analgesia

Analgesics

Anaphylaxis

Anxiety

Arthritis

Asthma

Atherosclerosis

Autoimmune disease

Burn

Cachexia

Cardiopulmonary bypass

Cirrhosis

Cystic fibrosis

Dermatitis

Diabetes mellitus

Drug dependence

Eczema

Encephalomyelitis

Epilepsy

Eye, disease

Headache

Heart, disease

Hepatitis

Infection

Inflammation

Intestine, disease

Ischemia

Liver, disease

Malaria

Meningitis

Multiple sclerosis

Myasthenia gravis

Neoplasm

Obesity

Osteoarthritis

Pain  
 Parkinson's disease  
 Psoriasis  
 Rheumatoid arthritis  
 Schizophrenia  
 Ulcer  
 Urticaria  
 (prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Drug delivery systems  
 (prodrugs; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Artery, disease  
 (restenosis; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Shock (circulatory collapse)  
 (septic; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Neoplasm  
 (solid; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Brain, disease  
 (stroke; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Functional groups  
 (sulfinate; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Functional groups  
 (sulfonamide; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Functional groups  
 (sulfonate group; prodrugs of NSAIDs contg. sulfur-contg. functional  
 groups for alleviation of side effects during therapy)

IT Functional groups  
 (sulfone; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Functional groups  
 (sulfoxide; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Functional groups  
 (sulfur-contg. groups; prodrugs of NSAIDs contg. sulfur-contg.  
 functional groups for alleviation of side effects during therapy)

IT Lupus erythematosus  
 (systemic; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT Shock (circulatory collapse)  
 (toxic shock syndrome; prodrugs of NSAIDs contg. sulfur-contg.  
 functional groups for alleviation of side effects during therapy)

IT Cytokines  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study,  
 unclassified); BIOL (Biological study)  
 (treatment with; prodrugs of NSAIDs contg. sulfur-contg. functional  
 groups for alleviation of side effects during therapy)

IT Intestine, disease  
 (ulcer; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Eye, disease  
 (uveitis; prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT Blood vessel, disease  
 (vasculitis; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT 329967-85-3, Cyclooxygenase 1



RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects during therapy)

IT 354145-55-4P 354145-61-2P 385369-37-9P 385369-40-4P 385369-42-6P  
 385369-44-8P 385369-45-9P 385369-47-1P 385369-48-2P 385369-49-3P  
 385369-50-6P 385369-51-7P 385369-52-8P 385369-53-9P 385369-54-0P  
 385369-56-2P 385369-57-3P 385369-58-4P 385369-63-1P 385369-64-2P  
 385369-65-3P 385369-66-4P 385369-68-6P 385369-69-7P 385369-70-0P  
**385369-71-1P** 385369-72-2P 385369-73-3P 385369-74-4P  
 385369-75-5P 385369-76-6P 385369-77-7P 385369-78-8P 385369-79-9P  
 385369-81-3P 385369-82-4P 385369-84-6P 385369-86-8P 385369-88-0P  
 385369-90-4P 385369-93-7P 385424-08-8P 385800-21-5P 385800-22-6P  
 385800-23-7P 385800-25-9P 385800-26-0P 385800-27-1P 385800-28-2P  
 444753-91-7P 444753-92-8P 444753-95-1P 444753-96-2P 444753-97-3P

RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation);  
**THU (Therapeutic use)**; BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (prepn. of prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects)

IT 63-74-1 70-55-3 80-17-1 98-09-9, Benzenesulfonyl chloride 98-59-9  
 98-68-0 98-74-8 107-15-3, 1,2-Ethanediamine, reactions 107-21-1,  
 Ethylene glycol, reactions 110-63-4, 1,4-Butanediol, reactions  
 111-29-5, 1,5-Pentanediol 111-46-6, Diethylene glycol, reactions  
 124-63-0, Methanesulfonyl chloride 138-39-6 421-83-0 504-63-2,  
 1,3-Propanediol 505-10-2 556-48-9, 1,4-Cyclohexanediol 594-44-5,  
 Ethanesulfonyl chloride 625-69-4, 2,4-Pentanediol 629-11-8,  
 1,6-Hexanediol 699-12-7 777-44-6 1120-71-4 1633-83-6 1950-68-1  
 2508-29-4, 5-Aminopentanol 2580-77-0 3144-09-0, Methanesulfonamide  
 3446-90-0 4048-33-3, 6-Amino-1-hexanol 5271-38-5 5455-59-4  
 5470-49-5 10210-17-0 13325-10-5, 4-Amino-1-butanol 15307-79-6  
 19690-37-0 20582-85-8 26159-34-2, Naproxen sodium 78521-69-4  
 385369-67-5 385800-24-8 444753-90-6 444753-93-9 444753-94-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects)

IT 16780-44-2P 87426-50-4P 106996-61-6P 120339-20-0P 126962-41-2P  
 156967-30-5P 156967-31-6P 184474-04-2P 214708-31-3P 354145-60-1P  
 385369-36-8P 385369-62-0P 385369-83-5P 385369-91-5P 385369-92-6P  
 385424-07-7P 385800-13-5P 385800-14-6P 385800-15-7P 385800-17-9P  
 385800-18-0P 385800-19-1P 385800-20-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of prodrugs of NSAIDs contg. sulfur-contg. functional groups  
 for alleviation of side effects)

IT 22204-53-1, Naproxen

RL: ADV (Adverse effect, including toxicity); BSU (Biological study,  
 unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or  
 reagent)  
 (prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
 alleviation of side effects during therapy)

IT 50-78-2, Aspirin 53-86-1, Indomethacin 54-21-7, Sodium salicylate  
 61-68-7, Mefenamic acid 103-90-2, Acetaminophen 552-94-3, Salsalate  
 2016-36-6, Choline salicylate, biological studies 5104-49-4,  
 Flurbiprofen 6385-02-0, Meclofenamate sodium 15307-86-5, Diclofenac  
 15687-27-1, Ibuprofen 18917-89-0, Magnesium salicylate 21256-18-8,  
 Oxaprozin 22071-15-4, Ketoprofen 22494-42-4, Diflunisal 23187-87-3,  
 Choline magnesium salicylate 26171-23-3, Tolmetin 31842-01-0,  
 Indoprofen 33005-95-7, Tiaprofenic acid 34597-40-5 36322-90-4,  
 Piroxicam 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8,  
 Nabumetone 51803-78-2, Nimesulide 53716-49-7, Carprofen 70374-39-9,  
 Lornoxicam 71125-38-7, Meloxicam 74103-07-4, Ketorolac tromethamine  
 80937-31-1, Flosulide

RL: ADV (Adverse effect, including toxicity); RCT (Reactant); BIOL

(Biological study); RACT (Reactant or reagent)  
(prodrugs of NSAIDs contg. sulfur-contg. functional groups for  
alleviation of side effects during therapy)

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Bjarnason, I; Gastroenterology 1993, V104, P1832 MEDLINE
- (2) Carson, J; Arch Intern Med 1987, V147, P1054 MEDLINE
- (3) Glaser, K; European J Pharm 1995, V281, P107 HCAPLUS
- (4) Graham, D; Clin Pharmacol Ther 1985, V38, P65 MEDLINE
- (5) Kaplan-Machlis, B; Annals of Pharmacotherapy 1999, V33, P979 HCAPLUS
- (6) Kargman, S; Gastroenterology 1996, V111, P445 HCAPLUS
- (7) Meade, E; J Biol Chem 1993, V268(9), P6610 HCAPLUS
- (8) Mitchell, J; Proc Natl Acad Sci USA 1994, V90, P11693
- (9) Onoe, Y; J Immunol 1996, V156, P758 HCAPLUS
- (10) Sakaki; US 6177466 B1 2001 HCAPLUS
- (11) Slater, D; Am J Obstet Gynecol 1995, V172, P77 HCAPLUS
- (12) Soll, A; Annals of Internal Medicine 1991, V114, P307 MEDLINE
- (13) Wallace, J; Gastroenterology 1997, V112, P1000 HCAPLUS

IT 385369-71-1P

RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

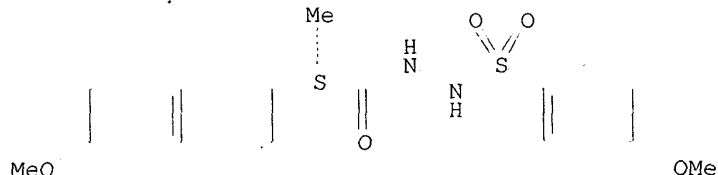
(Preparation); USES (Uses)

(prepn. of prodrugs of NSAIDs contg. sulfur-contg. functional groups  
for alleviation of side effects)

RN 385369-71-1 HCAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy-.alpha.-methyl-, 2-[(4-  
methoxyphenyl)sulfonyl]hydrazide, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:428855 HCAPLUS

DN 137:20228

TI Sulfonamido/amido/ureido-phenyl-amides as cyclophilin binding  
compounds

IN Hamilton, Gregory S.; Belyakov, Sergei; Vaal,  
Mark; Wei, Ling; Wu, Yong-Qian; Steiner,  
Joseph P.

PA Guilford Pharmaceuticals Inc., USA

SO PCT Int. Appl., 141 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C233-65

ICS C07C235-24; C07C235-56; C07C275-30; C07C275-36; C07C281-06;  
C07C309-73; C07C311-48; C07C311-49; C07C311-51; C07C335-20;  
C07C333-16; C07C335-18; C07C335-42; C07C337-06; C07C337-08;  
C07D207-16; C07D271-10; C07D285-12; C07D333-24

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid  
Compounds)

Section cross-reference(s): 1, 63

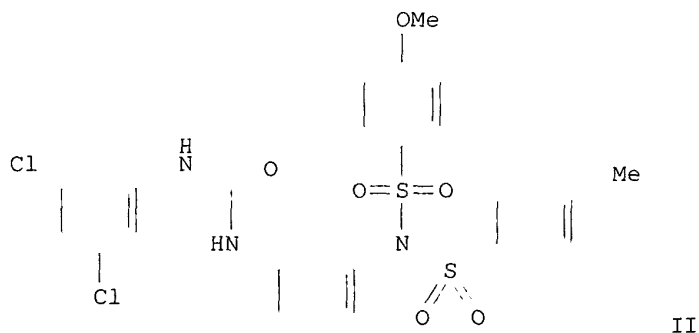
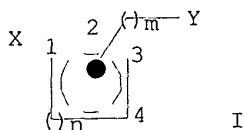
FAN.CNT 1

PATENT NO.

KIND DATE

APPLICATION NO. DATE

PI	WO 2002044126	A2	20020606	WO 2001-US44449	20011128
	WO 2002044126	A3	20020926		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002025767	A5	20020611	AU 2002-25767	20011128
	US 2002127605	A1	20020912	US 2001-994927	20011128
PRAI	US 2000-253074P	P	20001128		
	US 2001-291966P	P	20010521		
	WO 2001-US44449	W	20011128		
OS	MARPAT 137:20228				
GI					



AB Title compds. I [n = 1-2 forming a central 5-6 membered (un)satd. carbocyclic ring; m = 0-3; [CH<sub>2</sub>]<sub>m</sub>Y is attached to said central carbocyclic ring at position 2, 3, or 4; X, Y = carboxamide, thiocarboxamide, ureido, aminosulfonyl, etc.] were prepd. Examples include over 30 compds. synthesized, assays for rotamase inhibition, neuronal cell growth/regeneration, in-vivo protective effects in an animal model of stroke/myocardial infarction (rat) and an in-vivo model of hair growth (mouse). For instance, 3-nitroaniline was reacted with 4-methylphenylsulfonylsulfonyl chloride and 4-methoxyphenylsulfonyl chloride (DMA, Et<sub>3</sub>N) to give the bis(sulfonamide) as a solid. This intermediate was reduced (EtOHaq, NH<sub>4</sub>Cl, In.degree., reflux, 4 h) and subsequently treated with 3,5-dichlorophenylisocyanate to give II. II had IC<sub>50</sub> = 162 nM for rotamase (a measure of cyclophilin (

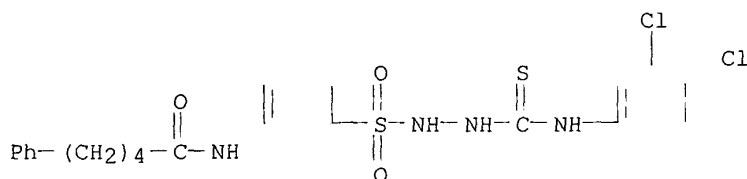
- CyP**) A binding). I have an affinity for **CyP**-type **immunophilin** proteins and are useful for the treatment of neurol. disorders, hair loss disorders, ischemic disorders, and disorders caused by viral or protozoan infection.
- ST sulfonamide urea formamide **cyclophilin** binding  
**immunophilin** prepn
- IT **Cyclophilins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(A; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nervous system  
(Guillain-Barre syndrome; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nervous system  
(Huntington's chorea; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nervous system  
(amyotrophic lateral sclerosis; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Alopecia  
(areata; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Mitochondria  
(blocking permeability transition pore in; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Ischemia  
(bowel; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Energy metabolism, animal  
(breakdown, inhibiting; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Cell death  
(calcium overload, prevention; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nervous system  
(cerebellar ataxia; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease  
(cerebral cortex, trauma; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease  
(cerebrovascular; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Anesthetics  
Anti-inflammatory agents  
Antibiotics  
(combination pharmaceutical; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Chemotherapy  
(combination therapy; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease  
(concussion; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Artery, disease  
(coronary; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Myelin  
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
(damage from laceration, compression, stretch, avulsion of peripheral nerves; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)

- IT Nervous system  
(degeneration; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nerve, disease  
(demyelination, central, peripheral; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nerve, disease  
(diabetic neuropathy; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Nervous system  
(disease; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Metabolism, animal  
(disorder, central/peripheral nervous system; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Hair preparations  
(dyes, combination pharmaceutical; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Heart, disease  
(failure; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Filaria  
(filariasis; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Infection  
(from pathogenic protozoan parasites; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Hair preparations  
(growth stimulants, combination pharmaceutical; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Hemorrhage  
(hematoma; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease  
(hemorrhagic stroke; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Coma  
(hypoglycemic; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Kidney
- Liverwort
- Spleen  
(infarction; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Axon
- Reperfusion
- Spinal cord  
(injury; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease
- Heart, disease
- Spinal cord  
(ischemia; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Leishmania  
(leishmaniasis from; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Alopecia  
(male pattern; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Metabolism, animal  
(mitochondrial, inhibition of; sulfonamido/amido/ureido-Ph-amides as

- cyclophilin binding compds.)**
- IT Nervous system  
(multiple system atrophy; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Anti-inflammatory agents  
(nonsteroidal, chemotherapy induced hair loss, treatment; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Nervous system  
(peripheral; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Eye, disease  
(photoreceptor, degeneration, treatment; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Transplant and Transplantation  
(reducing tissue damage; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Eye, disease  
(retinopathy, Ischemic; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Blood vessel, disease  
(retinopathy; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Onchocerca volvulus  
(river blindness from; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Schistosoma  
(schistosomiasis from; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Epilepsy  
(status epilepticus; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Brain, disease  
(stroke; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Alzheimer's disease  
Anti-Alzheimer's agents  
Anti-infective agents  
Antiglaucoma agents  
Antiparkinsonian agents  
Cardiovascular agents  
Cestoda  
Edema  
Eye, disease  
Glaucoma (disease)  
Human  
Human immunodeficiency virus  
Malaria  
Multiple sclerosis  
Nematoda  
Parkinson's disease  
Pinworm  
Wilson's disease  
(sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT **Cyclophilins**  
**Immunophilins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**
- IT Multiple sclerosis  
(therapeutic agents; sulfonamido/amido/ureido-Ph-amides as **cyclophilin binding compds.)**

- IT Toxoplasma gondii  
(toxoplasmosis from; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Brain, disease  
(trauma; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Infection  
(trypanosomiasis; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Infection  
(viral, neuropathy assocd. with; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT Adrenoceptor antagonists  
(.beta.-, chemotherapy induced hair loss, treatment; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT 59-05-2, Methotrexate  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(chemotherapy induced hair loss, treatment; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT 50-18-0, Cyclophosphamide 50-76-0, Dactinomycin 51-21-8,  
5-Fluorouracil 57-22-7, Vincristine 3778-73-2, Ifosfamide  
11056-06-7, Bleomycin 15663-27-1, Cisplatin 33069-62-4, Taxol  
33419-42-0, Etoposide 41575-94-4, Carboplatin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT 1995-43-3P 433976-82-0P, N-[3,5-Dichlorophenyl]-N'-[3-[[[4-methoxyphenyl]sulfonyl][[4-methylphenyl]sulfonyl]amino]phenyl]urea  
433976-83-1P 433976-84-2P 433976-85-3P 433976-86-4P,  
Bis[[3,5-dichlorophenyl]sulfonyl][3-[[[naphthylamino]thioxomethyl]amino]phenyl]amine 433976-87-5P 433976-88-6P 433976-89-7P 433976-90-0P  
433976-91-1P 433976-92-2P 433976-93-3P 433976-94-4P 433976-95-5P  
433976-96-6P 433976-97-7P 433976-98-8P 433976-99-9P 433977-00-5P  
433977-01-6P 433977-02-7P 433977-03-8P 433977-04-9P 433977-05-0P  
433977-06-1P 433977-07-2P 433977-08-3P 433977-09-4P 433977-10-7P  
433977-11-8P 433977-12-9P 433977-13-0P 433977-14-1P 433977-15-2P  
433977-16-3P 433977-17-4P 433977-18-5P 433977-19-6P 433977-20-9P  
433977-21-0P 433977-22-1P 433977-23-2P 433977-24-3P 433977-25-4P  
**433977-26-5P** 433977-27-6P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug; prepn. of 1,3-disubstituted sulfonamido/amido/ureido-Ph-amides as **immunophilin** ligands)
- IT 95076-93-0, Rotamase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; sulfonamido/amido/ureido-Ph-amides as **cyclophilin** binding compds.)
- IT 6398-87-4P 17722-36-0P 79023-02-2P 95425-81-3P, 3-[2,2-Bis(chlorophenyl)ethenyl]phenylamine 106109-72-2P 333440-82-7P  
433977-30-1P 433977-31-2P 433977-32-3P, N-(3,5-Dichlorophenyl)-2-(3-nitrophenoxy)acetamide 433977-33-4P, N-(3,5-Dichlorophenyl)-2-(3-aminophenoxy)acetamide 433977-34-5P, 2,3,4,5,6-Pentafluorobenzenesulfonic acid 3-aminophenyl ester 433977-35-6P,  
3-((3,5-Di(trifluoromethyl)benzyl)oxy)benzoic hydrazide 433977-36-7P  
433977-37-8P 433977-38-9P 433977-40-3P 433977-41-4P 433977-42-5P  
433977-43-6P, 4-((5-Phenylpentanoyl)amino)benzhydrazide 433977-44-7P  
433977-45-8P, N-[3-Aminobenzenesulfonyl]-N'-[tert-butylloxycarbonyl]hydrazine 433977-46-9P, N-[[3-[[5-Phenylpentanoyl]amino]benzene]sulfonyl]-N'-[tert-butylloxycarbonyl]hydrazine 433977-47-0P 433977-48-1P,  
3-[6-Phenylhexanoylamino]benzoic acid 433977-49-2P 433977-50-5P

- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (intermediate; prepn. of 1,3-disubstituted sulfonamido/amido/ureido-Ph-amides as **immunophilin** ligands)
- IT 433977-51-6 433977-52-7 433977-53-8 433977-54-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of 1,3-disubstituted sulfonamido/amido/ureido-Ph-amides as **immunophilin** ligands)
- IT 95-76-1, 3,4-Dichloroaniline 98-18-0, 3-Aminobenzenesulfonamide  
 99-06-9, 3-Hydroxybenzoic acid, reactions 99-09-2, 3-Nitroaniline  
 99-61-6, 3-Nitrobenzaldehyde 102-36-3, 3,4-Dichlorophenylisocyanate  
 121-51-7, 3-Nitrobenzenesulfonyl chloride 401-81-0, 3-Iodobenzotrifluoride 530-50-7, N,N-Diphenylhydrazine 582-33-2,  
 3-Aminobenzoic acid ethyl ester 591-19-5, 3-Bromoaniline 591-27-5,  
 3-Aminophenol 619-45-4, Methyl 4-aminobenzoate 626-43-7,  
 3,5-Dichloroaniline 705-21-5, 3,5-Dichlorophenylsulfonyl chloride  
 832-53-1, Pentafluorobenzenesulfonyl chloride 870-46-2,  
 tert-Butylcarbazate 1436-59-5, cis-1,2-Diaminocyclohexane 1878-88-2,  
 3-(Nitrophenoxy)acetic acid 2133-40-6, L-Proline methyl ester  
 hydrochloride 2270-20-4, 5-Phenylpentanoic acid 2905-62-6,  
 3,5-Dichlorobenzoyl chloride 3586-12-7, 3-Phenoxyaniline 4411-26-1  
 4518-10-9, Methyl 3-aminobenzoate 5581-75-9, 6-Phenylhexanoic acid  
 6590-93-8, 3,5-Dichlorophenylisothiocyanate 6590-94-9,  
 1,2-Dichloro-4-isothiocyanatobenzene 6952-67-6, 2-(3-Nitrophenyl)-1,3-dioxolane 14062-34-1, 3-Aminobenzoic acid hydrazide 16588-74-2  
 20371-41-9, 5-Phenylpentanoyl chloride 23165-29-9 31834-96-5, Hexynoic acid 32247-96-4, 3,5-Bis(trifluoromethyl)benzyl bromide 37517-81-0  
 161660-94-2 433977-28-7 433977-29-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; prepn. of 1,3-disubstituted sulfonamido/amido/ureido-Ph-amides as **immunophilin** ligands)
- IT 433977-26-5P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug; prepn. of 1,3-disubstituted sulfonamido/amido/ureido-Ph-amides as **immunophilin** ligands)
- RN 433977-26-5 HCAPLUS  
 CN Benzenesulfonic acid, 3-[(1-oxo-5-phenylpentyl)amino]-, 2-[[[(3,4-dichlorophenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



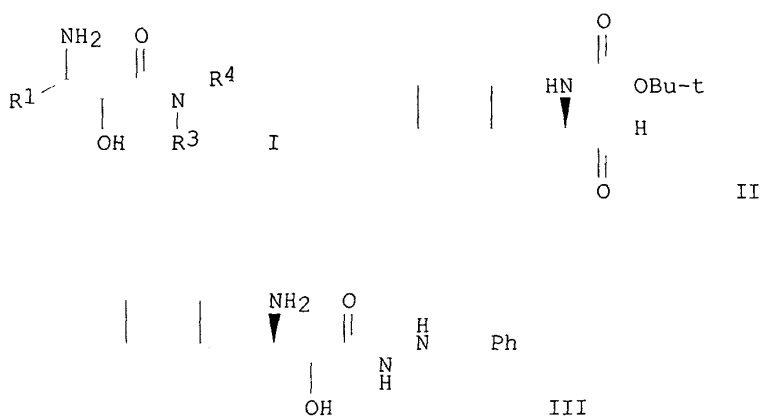
L48 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2002:11099 HCAPLUS  
 DN 136:69597  
 TI Synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors  
 IN Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.;  
 Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe  
 PA USA  
 SO U.S. Pat. Appl. Publ., 78 pp.  
 CODEN: USXXCO  
 DT Patent



LA English  
 IC ICM A61K031-47  
 ICS A61K031-166; C07C243-10; C07D215-38  
 NCL 514159000  
 CC 23-18 (Aliphatic Compounds)  
 Section cross-reference(s): 1, 25, 34

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002002152	A1	20020103	US 2001-833917	20010412
PRAI	US 2000-197262P	P	20000414		
OS	MARPAT 136:69597				
GI					



AB Title compds. I [R1 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R5S-alkylene; R3 = H, alkyl, arylalkyl; R4 = NR6R7, OR8; R5 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R6-7 = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxyalkonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R6-7 together are arylalkylidene; or R6-7 together with the nitrogen atom to which they are attached, form a heterocycle; R8 = H, alkanoylalkyl, alkenyl, alkoxyalkonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R9-10 = H, alkyl, aryl] were prepd. Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0.degree.C, room temp. 1 h) and oxidized to II (DMSO, Py.bul.SO3, Et3N, room temp. 30 min). II was converted to the bisulfite addn. product (H2O, NaHSO3, 5.degree.C, 24 h) and reacted with KCN to give the .alpha.-hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBT). Selected compds. I had IC50 < 0.1 .mu.M for MetAP2. I are useful for inhibiting angiogenesis.

ST hydrazide alkoxyamide angiogenesis inhibitors metap2 prepn

IT Angiogenesis inhibitors

(synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)

IT	369355-67-9P	369355-68-0P	369355-69-1P	369355-70-4P	369355-71-5P
	369355-72-6P	369355-73-7P	369355-74-8P	<b>369355-75-9P</b>	
	369355-76-0P	369355-77-1P	369355-78-2P	369355-79-3P	369355-80-6P
	369355-81-7P	369355-82-8P	369355-83-9P	369355-84-0P	369355-85-1P
	369355-86-2P	369355-87-3P	369355-88-4P	369355-89-5P	369355-90-8P
	369355-91-9P	369355-92-0P	369355-93-1P	369355-94-2P	369355-95-3P

369355-96-4P	369355-97-5P	369355-98-6P	369355-99-7P	369356-00-3P
369356-01-4P	369356-02-5P	369356-03-6P	369356-04-7P	369356-05-8P
369356-06-9P	369356-07-0P	369356-08-1P	369356-09-2P	369356-10-5P
369356-11-6P	369356-12-7P	369356-13-8P	369356-14-9P	369356-15-0P
369356-16-1P	369356-17-2P	369356-18-3P	369356-19-4P	369356-20-7P
369356-21-8P	369356-22-9P	369356-23-0P	369356-24-1P	369356-25-2P
369356-26-3P	369356-27-4P	369356-28-5P	369356-29-6P	369356-30-9P
369356-31-0P	369356-32-1P	369356-33-2P	369356-34-3P	369356-35-4P
369356-36-5P	369356-37-6P	369356-38-7P	369356-39-8P	369356-40-1P
369356-41-2P	369356-42-3P	369356-43-4P	369356-44-5P	369356-45-6P
369356-46-7P	369356-47-8P	369356-48-9P	369356-49-0P	369356-50-3P
369356-51-4P	369356-52-5P	369356-53-6P	369356-54-7P	369356-55-8P
369356-56-9P	369356-57-0P	369356-58-1P	369356-59-2P	369356-60-5P
369356-61-6P	369356-62-7P	369356-63-8P	369356-64-9P	369356-65-0P
369356-66-1P	369356-67-2P	369356-68-3P	369356-69-4P	369356-70-7P
369356-71-8P	369356-72-9P	369356-73-0P	369356-74-1P	369356-75-2P
369356-76-3P	369356-77-4P	369356-78-5P	369356-79-6P	369356-80-9P
369356-81-0P	369356-82-1P	369356-83-2P	369356-84-3P	369356-85-4P
369356-86-5P	369356-87-6P	369356-88-7P	369356-89-8P	369356-90-1P
369356-91-2P	369356-92-3P	369356-93-4P	369356-94-5P	369356-95-6P
369356-96-7P	369356-97-8P	369356-98-9P	369356-99-0P	369357-00-6P
369357-01-7P	369357-02-8P	369357-03-9P	369357-04-0P	369357-05-1P
369357-06-2P	369357-07-3P	369357-08-4P	369357-09-5P	369357-10-8P
369357-11-9P	369357-12-0P	369357-13-1P	369357-14-2P	369357-15-3P
369357-16-4P	369357-17-5P	369357-18-6P	369357-19-7P	369357-20-0P
369357-21-1P	369357-22-2P	369357-23-3P	369357-24-4P	369357-25-5P
369357-26-6P	369357-27-7P	369357-28-8P	369357-29-9P	369357-30-2P
369357-32-4P	369357-34-6P	369357-36-8P	369357-38-0P	369357-40-4P
369357-42-6P	369357-44-8P	369357-46-0P	369357-48-2P	369357-50-6P
369357-51-7P	369357-52-8P	369357-53-9P	369357-54-0P	369357-56-2P
369357-58-4P	369357-60-8P	369357-62-0P	369357-64-2P	369357-66-4P
369357-68-6P	369357-69-7P	369357-70-0P	369357-71-1P	369357-72-2P
369357-73-3P	369357-74-4P	369357-75-5P	369357-76-6P	369357-77-7P
369357-78-8P	369357-79-9P	369357-80-2P	369357-81-3P	369357-82-4P
369357-83-5P	369357-84-6P	369357-85-7P	369357-86-8P	369357-87-9P
369357-88-0P	369357-89-1P	369357-90-4P	369357-91-5P	369357-92-6P
369357-93-7P	369357-94-8P	369357-95-9P	369357-96-0P	369357-97-1P
369357-98-2P	369357-99-3P	369358-00-9P	369358-01-0P	369358-02-1P
369358-03-2P	369358-04-3P	369358-05-4P	369358-06-5P	369358-07-6P
369358-08-7P	369358-09-8P	369358-10-1P	369358-11-2P	369358-12-3P
369358-13-4P	369358-14-5P	369358-15-6P	369358-16-7P	369358-17-8P
369358-18-9P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
inhibitors)

IT 369358-19-0P	369358-20-3P	369358-21-4P	369358-22-5P	369358-23-6P
369358-24-7P	369358-25-8P	369358-26-9P	369358-27-0P	369358-28-1P
369358-29-2P	369358-30-5P	369358-31-6P	369358-32-7P	369358-33-8P
369358-34-9P	369358-35-0P	369358-37-2P	369358-38-3P	369358-40-7P
369358-41-8P	369358-42-9P	369358-43-0P	369358-44-1P	369358-45-2P
369358-46-3P	369358-48-5P	369358-50-9P	369358-52-1P	369358-53-2P
369358-54-3P	369358-55-4P	369358-57-6P	369358-59-8P	369358-60-1P
369358-61-2P	369358-62-3P	369358-63-4P	369358-64-5P	369358-65-6P
369358-66-7P	369358-67-8P	369358-68-9P	369358-69-0P	369358-70-3P
369358-71-4P	369358-72-5P	369358-73-6P	369358-74-7P	369358-75-8P
369358-76-9P	369358-77-0P	369358-78-1P	369358-79-2P	369358-80-5P
369358-81-6P	369358-82-7P	369358-83-8P	369358-84-9P	369358-85-0P
369358-86-1P	369358-87-2P	369358-88-3P	369358-89-4P	369358-90-7P
369358-91-8P	369358-92-9P	369358-93-0P	369358-94-1P	369358-95-2P
369358-96-3P	369358-97-4P	369358-98-5P	369358-99-6P	369359-00-2P
369359-01-3P	369359-02-4P	369359-03-5P	369359-04-6P	369359-05-7P

369359-06-8P 369359-07-9P 369359-08-0P 369359-09-1P 369359-10-4P  
 369359-11-5P 369359-12-6P 369359-13-7P 369359-14-8P 369359-15-9P  
 369359-16-0P 369359-17-1P 369359-18-2P 369359-19-3P 369359-20-6P  
 369359-21-7P 369359-22-8P 369359-23-9P 369359-24-0P 369359-25-1P  
 369359-26-2P 369359-27-3P 369359-28-4P 369359-29-5P 369359-30-8P  
 369359-31-9P 369359-32-0P 369359-33-1P 369359-34-2P 369359-35-3P  
 369359-36-4P 369359-37-5P 369359-38-6P 369359-39-7P 369359-40-0P  
 369359-41-1P 369359-42-2P 369359-43-3P 369359-44-4P 369359-45-5P  
 369359-46-6P 369359-47-7P 369359-48-8P 369359-49-9P  
**369359-50-2P** 369359-51-3P 369359-52-4P 369359-53-5P  
 369359-55-7P 369359-56-8P 369359-57-9P 369359-58-0P 369359-59-1P  
 369359-60-4P 369359-61-5P 369359-62-6P 369359-63-7P 369359-64-8P  
 369359-65-9P 369359-66-0P 369359-67-1P 369359-68-2P 369359-69-3P  
 369359-71-7P 369359-72-8P 369359-73-9P 369359-74-0P 369359-75-1P  
 369359-76-2P 369359-77-3P 369359-78-4P 369359-79-5P 369359-80-8P  
 369359-81-9P 369359-82-0P 369359-83-1P 369359-84-2P 369359-85-3P  
 369359-86-4P 369359-87-5P 369359-88-6P 369359-89-7P 369359-90-0P  
 369359-91-1P 369359-92-2P 369359-93-3P 369359-94-4P 369359-95-5P  
 369359-96-6P 369359-97-7P 369359-98-8P 369359-99-9P 369360-00-9P  
 369360-01-0P 369360-02-1P 369360-03-2P 369360-04-3P 369360-05-4P  
 369360-06-5P 369360-07-6P 369360-08-7P 369360-09-8P 369360-10-1P  
 369360-11-2P 369360-12-3P 369360-13-4P 369360-14-5P 369360-15-6P  
 369360-16-7P 369360-17-8P 369360-18-9P 369360-19-0P 369360-20-3P  
 369360-21-4P 369360-22-5P 369360-23-6P 369360-24-7P 369360-25-8P  
 369360-26-9P 369360-27-0P 369360-28-1P 369360-29-2P 369360-30-5P  
 369360-31-6P 369360-32-7P 369360-33-8P 369360-34-9P 369360-35-0P  
 369360-36-1P 369360-37-2P 369360-38-3P 369360-39-4P 369360-40-7P  
 369360-41-8P 369360-42-9P 369360-43-0P 369360-44-1P 369360-45-2P  
 369360-46-3P 369360-47-4P 369360-48-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU**  
**(Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
 inhibitors)

IT 585-71-7P 18328-11-5P, Benzenebutanal 39684-80-5P,  
 N-(tert-Butoxycarbonyl)-2-bromoethylamine 52245-11-1P 58634-67-6P  
 67032-33-1P, Methyl 3-(2,3-dihydroxypropyloxy)benzoate 68432-92-8P,  
 Methyl 3-(cyanomethyl)benzoate 71925-14-9P 79250-46-7P, Methyl  
 3-(prop-2-enyloxy)benzoate 110238-61-4P 129593-17-5P 148433-10-7P,  
 Methyl 3-propoxybenzoate 160820-17-7P 172789-09-2P 339592-56-2P  
 360788-02-9P, 3-(3-Indolyl)propanal 369360-49-6P 369360-50-9P  
 369360-51-0P 369360-52-1P 369360-53-2P 369360-54-3P 369360-55-4P  
 369360-56-5P 369360-57-6P 369360-58-7P 369360-59-8P 369360-60-1P  
 369360-61-2P 369360-62-3P 369360-63-4P 369360-64-5P 369360-65-6P  
 369360-66-7P 369360-67-8P 369360-68-9P 369360-69-0P 369360-70-3P  
 369360-71-4P 369360-72-5P, Ethyl 4-ethyloct-2-enoate 369360-73-6P  
 369360-74-7P 369360-75-8P 369360-76-9P 369360-77-0P 369360-78-1P  
 369360-79-2P 369360-80-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(intermediate; synthesis of hydrazide and .alpha.-alkoxyamide  
 angiogenesis inhibitors)

IT 50-45-3, 2,3-Dichlorobenzoic acid 50-79-3, 2,5-Dichlorobenzoic acid  
 50-84-0, 2,4-Dichlorobenzoic acid 51-36-5, 3,5-Dichlorobenzoic acid  
 51-44-5, 3,4-Dichlorobenzoic acid 51-71-8, 1-(2-Phenethyl)hydrazine  
 55-22-1, 4-Pyridinecarboxylic acid, reactions 64-04-0,  
 2-Phenylethylamine 69-72-7, 2-Hydroxybenzoic acid, reactions 74-11-3,  
 4-Chlorobenzoic acid 75-26-3, 2-Bromopropane 78-77-3,  
 1-Bromo-2-methylpropane 79-31-2, 2-Methylpropionic acid 86-55-5,  
 1-Naphthoic acid 86-87-3, 1-Naphthylacetic acid 88-13-1,  
 3-Thiophenecarboxylic acid 88-14-2, Furan-2-carboxylic acid 88-65-3,  
 2-Bromobenzoic acid 91-40-7, N-Phenylanthranilic acid 91-52-1,  
 2,4-Dimethoxybenzoic acid 93-07-2, 3,4-Dimethoxybenzoic acid 93-25-4,

2-Methoxyphenylacetic acid 94-53-1, 1,3-Benzodioxole-5-carboxylic acid  
98-73-7, 4-tert-Butylbenzoic acid 98-85-1 98-89-5,  
Cyclohexanecarboxylic acid 98-97-5, 2-Pyrazine carboxylic acid  
98-98-6, 2-Pyridinecarboxylic acid 99-04-7, 3-Methylbenzoic acid  
99-05-8, 3-Aminobenzoic acid 99-06-9, 3-Hydroxybenzoic acid, reactions  
99-64-9, 3-Dimethylaminobenzoic acid 99-94-5, 4-Methylbenzoic acid  
99-96-7, 4-Hydroxybenzoic acid, reactions 100-09-4, 4-Methoxybenzoic  
acid 100-63-0, 1-Phenylhydrazine 103-82-2, Phenylacetic acid,  
reactions 104-01-8, 4-Methoxyphenylacetic acid 104-88-1,  
4-Chlorobenzaldehyde, reactions 106-94-5, 1-Bromopropane 111-14-8,  
Heptanoic acid 118-41-2, 3,4,5-Trimethoxybenzoic acid, reactions  
118-90-1, 2-Methylbenzoic acid 118-91-2, o-Chlorobenzoic acid  
118-92-3, 2-Aminobenzoic acid 134-11-2, 2-Ethoxybenzoic acid 150-13-0,  
4-Aminobenzoic acid 349-46-2, D-Cystine 368-78-5 368-90-1,  
1-[4-(Trifluoromethyl)phenyl]hydrazine 371-14-2, 1-(4-  
Fluorophenyl)hydrazine 445-29-4, 2-Fluorobenzoic acid 454-92-2,  
3-(Trifluoromethyl)benzoic acid 455-24-3, 4-(Trifluoromethyl)benzoic  
acid 455-38-9, 3-Fluorobenzoic acid 456-22-4, 4-Fluorobenzoic acid  
488-93-7, Furan-3-carboxylic acid 499-06-9, 3,5-Dimethylbenzoic acid  
501-81-5, 3-Pyridylacetic acid 503-74-2, 3-Methylbutyric acid  
524-38-9, N-Hydroxyphthalimide 527-72-0, 2-Thiophenecarboxylic acid  
530-50-7 536-40-3, 4-Chlorobenzohydrazide 536-66-3, 4-Isopropylbenzoic  
acid 537-47-3, N-Phenylhydrazinecarboxamide 539-44-6,  
1-(4-Methylphenyl)hydrazine 556-08-1, 4-Acetamidobenzoic acid  
579-75-9, o-Anisic acid 581-96-4, 2-Naphthylacetic acid 585-76-2,  
3-Bromobenzoic acid 586-38-9, 3-Methoxybenzoic acid 586-76-5,  
4-Bromobenzoic acid 589-21-9, 1-(4-Bromophenyl)hydrazine 593-56-6,  
O-Methylhydroxylamine hydrochloride 603-79-2, 2,3-Dimethylbenzoic acid  
610-72-0, 2,5-Dimethylbenzoic acid 611-01-8, 2,4-Dimethylbenzoic acid  
612-35-1, .alpha.-Phenyl-o-toluic acid 613-94-5, Benzohydrazide  
615-21-4 618-40-6, 1-Methyl-1-phenylhydrazine 619-04-5,  
3,4-Dimethylbenzoic acid 619-64-7, 4-Ethylbenzoic acid 619-65-8,  
4-Cyanobenzoic acid 619-84-1, 4-Dimethylaminobenzoic acid 619-86-3,  
4-Ethoxybenzoic acid 622-36-6, 1-(2-Methylphenyl)hydrazine 634-97-9,  
2-Pyrrole carboxylic acid 636-10-2, 1-(3-Methylbutyl)-1-phenylhydrazine  
636-44-2, 2,5-Dimethyl-3-furoic acid 636-97-5, 4-Nitrobenzohydrazide  
637-80-9, Ethyl hydrazinoacetate 644-21-3, 1-Ethyl-1-phenylhydrazine  
658-27-5, 1-(3-Fluorophenyl)hydrazine 699-90-1, 3-Fluoro-2-methylbenzoic  
acid 771-61-9, Pentafluorophenol 825-99-0, 3-(Methylthio)benzoic acid  
830-96-6, 1H-Indole-3-propanoic acid 867-13-0, Triethyl phosphonoacetate  
870-46-2, tert-Butyl hydrazinecarboxylate 1014-81-9,  
3-(Trifluoromethoxy)benzoic acid 1073-69-4, 1-(4-Chlorophenyl)hydrazine  
1115-59-9, L-Alanine ethyl ester hydrochloride 1123-00-8,  
Cyclopentylacetic acid 1129-28-8, Methyl 3-(bromomethyl)benzoate  
1132-21-4, 3,5-Dimethoxybenzoic acid 1438-16-0, 3-Amino-2-thioxo-1,3-  
thiazolidin-4-one 1452-63-7 1498-96-0, 4-Butoxybenzoic acid  
1521-38-6, 2,3-Dimethoxybenzoic acid 1538-08-5 1576-35-8,  
4-Methylphenylsulfonylhydrazine 1621-91-6, 1H-Pyrazole-5-carboxylic acid  
1673-47-8, 3-Chlorobenzohydrazide 1798-09-0, 3-Methoxyphenylacetic acid  
1821-12-1, 4-Phenylbutyric acid 1877-72-1, 3-Cyanobenzoic acid  
1878-65-5, 3-Chlorophenylacetic acid 1878-66-6, 4-Chlorophenylacetic  
acid 1918-79-2, 5-Methylthiophene-2-carboxylic acid 2164-61-6,  
3-Pyridazine carboxylic acid 2213-43-6, 1-Aminopiperidine 2215-77-2,  
4-Phenoxybenzoic acid 2243-55-2, 1-Naphthylhydrazine 2361-27-5,  
2-Thiophenecarbohydrazide 2368-80-1, 1-(2-Fluorophenyl)hydrazine  
2438-05-3, 4-n-Propylbenzoic acid 2444-36-2, 2-Chlorophenylacetic acid  
2550-36-9, (Bromomethyl)cyclohexane 2576-47-8, 2-Bromoethylamine  
hydrobromide 2687-43-6, O-Benzylhydroxylamine hydrochloride 2785-98-0,  
2,5-Dimethoxybenzoic acid 3235-69-6, 4-Morpholineacetic acid  
3332-29-4, O-Ethylhydroxylamine hydrochloride 3400-45-1,  
Cyclopentanecarboxylic acid 3438-16-2, 5-Chloro-2-methoxybenzoic acid  
3471-32-7, 1-(4-Methoxyphenyl)hydrazine 3619-22-5, 4-  
Methylbenzohydrazide 3839-22-3, 2-Cyanobenzoic acid 3919-73-1,

O-(Carboethoxy)methylhydroxylamine hydrochloride 3973-08-8, 4-Thiazole  
 carboxylic acid 4052-30-6, 4-(Methylsulfonyl)benzoic acid 4361-28-8,  
 3-Cyclohexylpropanal 4392-54-5, 4-Hydrazinobenzenesulfonamide  
 4519-39-5, 2,3-Difluorobenzoic acid 4761-00-6, 2,4,6-Trimethylbenzyl  
 bromide 4846-21-3, O-Phenylhydroxylamine 4890-85-1,  
 2-Bibenzylcarboxylic acid 4930-98-7, 2-Hydrazinopyridine 5042-30-8,  
 1-(2,2,2-Trifluoroethyl)hydrazine 5292-21-7, Cyclohexylacetic acid  
 5331-43-1, Benzyl carbazate 5341-58-2, 3-Hydroxy-2-naphthoylhydrazine  
 5409-31-4, 3,4-Diethoxybenzoic acid 5429-28-7, 4-(Diethylamino)benzoic  
 acid 5438-19-7, 4-Propoxybenzoic acid 5537-74-6, 3-(Ethylthio)benzoic  
 acid 5728-52-9, 4-Phenylphenylacetic acid 5785-06-8,  
 3-Methoxybenzohydrazide 5814-05-1, 2-Chlorobenzohydrazide 5818-06-4,  
 3-Hydroxybenzoyl hydrazide 6027-14-1, D-Homocysteine 6084-58-8,  
 O-Isobutylhydroxylamine hydrochloride 6092-80-4, O-Phenylhydroxylamine  
 hydrochloride 6498-34-6, 1-Cyclohexylhydrazine 6638-79-5,  
 N,O-Dimethylhydroxylamine hydrochloride 6688-11-5, Cyclooctanealdehyde  
 6973-60-0, 1-Methylpyrrole-2-carboxylic acid 7466-54-8,  
 2-Methoxybenzohydrazide 10449-07-7, 1-(2-Chlorophenyl)hydrazine  
 13050-47-0, 3-Methylbenzohydrazide 13115-43-0, 2-Pyridylacetic acid  
 13116-27-3, 1-(4-Iodophenyl)hydrazine 13205-46-4, 4-Isopropoxybenzoic  
 acid 13205-48-6, 4-Methylthiobenzoic acid 13205-49-7,  
 4-(Ethylthio)benzoic acid 13205-50-0, 4-(Isopropylthio)benzoic acid  
 13221-86-8, 2,4-Dihydroxybenzohydrazide 13636-54-9, 1-Mesitylhydrazine  
 13957-54-5, 14190-59-1, 2-Thiazole carboxylic acid 14527-41-4,  
 5-Thiazolecarboxylic acid 14763-20-3, 1-(3-Chlorophenyl)hydrazine  
 15384-39-1, 1-(3-Methoxyphenyl)hydrazine 16182-15-3, 16596-41-1,  
 1-Pyrrolidinamine 16874-33-2, 2-Tetrahydrofuroic acid 17078-28-3,  
 4-Dimethylaminophenylacetic acid 17284-97-8, 3-Chloro-6-  
 hydrazinopyridazine 17894-25-6, 2,5-Dimethoxybenzohydrazide 19275-55-9  
 19438-10-9, Methyl 3-hydroxybenzoate 20570-96-1, 21169-71-1,  
 5-Isoxazolecarboxylic acid 22026-39-7, 22683-48-3, 4-  
 (Propylthio)benzoic acid 22683-49-4, 4-(Butylthio)benzoic acid  
 22683-51-8, 4-(Hexylthio)benzoic acid 22855-95-4, 4-(Benzylthio)benzoic  
 acid 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23834-14-2,  
 7-Chloro-4-hydrazinoquinoline 25503-90-6, 1-Acetylpiperidine-4-  
 carboxylic acid 28356-58-3, 4-Pyridylacetic acid 30923-92-3,  
 1-(Cyclopentyl)hydrazine 30963-12-3, 2-(1-Methylhydrazino)-3-  
 nitropyridine 31462-59-6, 4-Pyrimidine carboxylic acid 31719-76-3,  
 4-(Phenoxymethyl)benzoic acid 32443-99-5, D-Cysteine hydrochloride  
 32910-52-4, 4-(Cyclohexylthio)benzoic acid 32910-56-8,  
 4-(4-Methylpentylthio)benzoic acid 32910-70-6, 4-(2-  
 Cyclohexylethylthio)benzoic acid 36239-09-5, Ethyl-3-chloro-3-oxo  
 propionate 36331-57-4, Benzylsulfonylhydrazine 37718-11-9,  
 1H-Pyrazole-4-carboxylic acid 37860-70-1, 2,3-Diethoxybenzoic acid  
 38945-21-0, O-Allylhydroxylamine hydrochloride 39115-96-3,  
 3-Bromobenzohydrazide 39627-84-4, 2-Naphthoylhydrazine 39684-28-1,  
 O-tert-Butylhydroxylamine hydrochloride 39943-56-1, 1-(3,5-  
 Dichlorophenyl)hydrazine 40594-30-7, 1-(2,4-Difluorophenyl)hydrazine  
 40887-80-7, 1-(3-Bromophenyl)hydrazine 43038-45-5, 1-Naphthoylhydrazine  
 46230-31-3, O-(Carbobenzyloxy)methylhydroxylamine 51304-65-5,  
 1-(3-Chloro-4-methylphenyl)hydrazine 51421-13-7, 1-(2-  
 Chlorobenzyl)hydrazine 51546-12-4, 2-Chloro-5-(methylthio)benzoic acid  
 51707-38-1, 3,5-Dimethoxybenzohydrazide 53516-97-5, 3-  
 Chlorophenylsulfonylhydrazine 53551-35-2, 4-(2-Methylpropylthio)benzoic  
 acid 54699-92-2, 58586-81-5, 4-Ethoxybenzohydrazide 58791-94-9,  
 1-(4-Chloro-2-methylphenyl)hydrazine 59983-39-0, (2S)-2-(Methoxymethyl)-  
 1-pyrrolidinamine 60739-40-4, 3-(Benzylthio)benzoic acid 61645-34-9,  
 2-Hydrazinoquinoxaline 61715-74-0, 1-Propyl-1-phenylhydrazine  
 62524-21-4

RL: RCT (Reactant); RACT (Reactant or reagent)

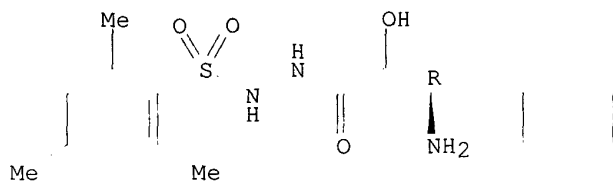
(reactant; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
 inhibitors)

IT 63693-65-2, 1-(4-Isopropylphenyl)hydrazine 65227-54-5,

1-Naphthylsulfonylhydrazine 66971-55-9, 5-Hydrazino-1,3-dimethyl-4-nitro-1H-pyrazole 67487-35-8, 2,5-Dichlorobenzohydrazide 70491-05-3, (2R)-2-[(tert-Butoxycarbonyl)amino]-2-(cyclohexyl)ethanoic acid 71056-18-3, 1-(Cyclopropylmethyl)-1-phenylhydrazine 72748-99-3, (2R)-2-(Methoxymethyl)-1-pyrrolidinamine 73469-90-6 75681-13-9, Methyl 3-hydrazino-2-thiophenecarboxylate 76953-33-8, 3-Chloro-6-(1-methylhydrazino)pyridazine 79786-62-2, 1-Octyl-1-phenylhydrazine 82732-07-8, (2R)-2-[(tert-Butoxycarbonyl)amino]-4-phenylbutanoic acid 83823-06-7, 6-Chloro(2H)-1-benzopyran-3-carboxylic acid 84282-78-0, 3-Chloro-4-fluorophenylhydrazine 88561-15-3, 1-Hexyl-1-phenylhydrazine 89364-31-8 96017-23-1, 4-Chloro-2-methyl-5-(1-methylhydrazino)-3(2H)-pyridazinone 97108-50-4, 1-(2,5-Difluorophenyl)hydrazine 104636-55-7, 1-(3-Phenylpropyl)-1-phenylhydrazine 106087-14-3, 1-(2-Methylpropyl)-1-phenylhydrazine 108329-74-4, (2R)-2-[(tert-Butoxycarbonyl)amino]-4-(ethylthio)butanoic acid 110208-00-9, 3-(Propylthio)benzoic acid 114670-74-5 114838-12-9, 3-(Isopropylthio)benzoic acid 127095-92-5, (2R)-2-[(tert-Butoxycarbonyl)amino]-3-cyclohexylpropanoic acid 140853-10-7 163620-24-4, 2-(1-Methylhydrazino)-5-(trifluoromethyl)pyridine 170162-56-8, 3-(Butylthio)benzoic acid 172516-47-1 175137-28-7, Methyl 2-hydrazino-4-(trifluoromethyl)-5-pyrimidinecarboxylate 175137-33-4 175276-74-1, 1-(2-Chloro-6-fluorophenyl)hydrazine 207974-22-9, N-(4-Chloro-2-methoxyphenyl)hydrazinecarboxamide 240407-62-9 369360-81-6 369360-82-7 369360-83-8 369360-84-9, 1-Pentyl-1-phenylhydrazine 369360-85-0, 1-(2-Methylbutyl)-1-phenylhydrazine 369360-86-1, 1-(2-Methylpentyl)-1-phenylhydrazine 369360-87-2, 1-(3-Methylpentyl)-1-phenylhydrazine 369360-88-3, 1-(3,3-Dimethylbutyl)-1-phenylhydrazine 369360-89-4, 1-(2-Ethylbutyl)-1-phenylhydrazine 369360-90-7, 1-Dodecyl-1-phenylhydrazine 369360-91-8, 1-(3,5,5-Trimethylhexyl)-1-phenylhydrazine 369360-92-9, 1-(2-Benzoyloxyethyl)-1-phenylhydrazine 369360-93-0, 1-(2,2,5-Trichloropentyl)-1-phenylhydrazine 369360-94-1, 1-Heptyl-1-phenylhydrazine 369360-95-2, 1-[3-(Methylthio)propyl]-1-phenylhydrazine 369360-96-3, 1-(Cyclopentylmethyl)-1-phenylhydrazine 369360-97-4, 1-(5-Hydroxypentyl)-1-phenylhydrazine 369360-98-5, 1-((2R)-2,3-Dihydroxypropyl)-1-phenylhydrazine 369360-99-6, 1-(2,2-Dichlorohexyl)-1-phenylhydrazine 369361-00-2, 1-(7-Methoxy-3,7-dimethyloctyl)-1-phenylhydrazine 369361-01-3, 1-[2-(4-Methylphenyl)ethyl]-1-phenylhydrazine 369361-02-4, 1-(2-Ethylhexyl)-1-phenylhydrazine 369361-03-5, 1-[2-(4-Chlorophenyl)-2-cyanoethyl]-1-phenylhydrazine 369361-04-6, 1-(2-Phenylpropyl)-1-phenylhydrazine 369361-05-7, 1-(Cyclooctylmethyl)-1-phenylhydrazine 369361-06-8, 1-[(11Z)-1-Hexadecenyl]-1-phenylhydrazine 369361-07-9, 1-Tridecyl-1-phenylhydrazine 369361-08-0, 4-(1-Phenylhydrazino)butanoic acid 369361-09-1, 1-((6Z)-6-Nonenyl)-1-phenylhydrazine 369361-10-4, 1-((4Z)-4-Decenyl)-1-phenylhydrazine 369361-11-5, 1-(4-Pentenyl)-1-phenylhydrazine 369361-12-6, 1-(3,7-Dimethyl-6-octenyl)-1-phenylhydrazine 369361-13-7, 1-(4,4,4-Trifluorobutyl)-1-phenylhydrazine 369361-14-8, 1-(3-Hydroxybutyl)-1-phenylhydrazine 369361-15-9, 1-[2-[(3,7-Dimethyl-6-octenyl)oxy]ethyl]-1-phenylhydrazine 369361-16-0, 1-[2-(3,3-Dimethylcyclohexyl)ethyl]-1-phenylhydrazine 369361-17-1, 1-((4S)-6-Bromo-4-methylhexyl)-1-phenylhydrazine 369361-18-2, 1-Cyclohexylmethyl-1-phenylhydrazine 369361-19-3, 3-(Hexylthio)benzoic acid 369361-20-6, 3-(2-Methylpropylthio)benzoic acid 369361-21-7, 3-(4-Methylpentylthio)benzoic acid 369361-22-8, 3-(1-Methylpropylthio)benzoic acid 369361-23-9, 3-(2,2-Dimethylpropylthio)benzoic acid 369361-24-0, 3-(Cyclohexylthio)benzoic acid 369361-25-1, 3-(2-Cyclohexylethylthio)benzoic acid 369361-26-2, 3-(2-Phenylethylthio)benzoic acid 369361-27-3, 3-(3-Phenylpropylthio)benzoic acid 369361-28-4 369361-29-5, 4-(1-Methylpropylthio)benzoic acid 369361-30-8, 4-(2,2-Dimethylpropylthio)benzoic acid 369361-31-9, 4-(2-Phenylethylthio)benzoic acid 369361-32-0, 4-(3-Phenylpropylthio)benzoic acid 369361-33-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)  
 IT 61229-81-0, Methionine aminopeptidase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (type 2; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)  
 IT 369355-75-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)  
 RN 369355-75-9 HCAPLUS  
 CN Cyclohexanebutanoic acid, .beta.-amino-.alpha.-hydroxy-, 2-[(2,4,6-trimethylphenyl)sulfonyl]hydrazide, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2002:10229 HCAPLUS  
 DN 136:85672  
 TI Modified forms of pharmacologically active agents for use as nonsteroidal anti-inflammatory drugs (NSAIDs)  
 IN Lai, Ching-san; Wang, Tingmin  
 PA Medinox, Inc., USA  
 SO PCT Int. Appl., 74 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K  
 CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1, 27, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002000167	A2	20020103	WO 2001-US19750	20010619
	WO 2002000167	A3	20020404		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6355666	B1	20020312	US 2000-602688	20000623
	US 6429223	B1	20020806	US 2000-715767	20001117
	AU 2001070010	A5	20020108	AU 2001-70010	20010619
PRAI	US 2000-602688	A1	20000623		

US 2000-715767 A1 20001117  
 WO 2001-US19750 W 20010619  
 OS MARPAT 136:85672  
 GI



- AB In accordance with the present invention, there are provided modified forms of nonsteroidal anti-inflammatory drugs (NSAIDs), X-L-Z [X = non-steroidal anti-inflammatory drug (NSAID); L = optional linker/spacer, WR; Z = sulfur-contg. functional group contg. an (un)substituted hydrocarbon; R = (un)substituted alkylene, cycloalkylene, heterocyclic, oxyalkylene, alkenylene, arylene, alkarylene; W = ester, reverse ester, thioester, reverse thioester, amide, reverse amide, phosphate, phosphonate, imine, enamine]. Thus, naproxen (I; R = H) was esterified with propane-1,3-diol in CHCl<sub>3</sub> contg. catalytic p-tosic acid followed by sulfonation with tosyl chloride in pyridine to give prodrug I [R = (CH<sub>2</sub>)<sub>3</sub>OSO<sub>2</sub>C<sub>4</sub>H<sub>4</sub>Me-4 (II)]. Modified NSAIDs according to the invention provide a new class of anti-inflammatory agent which provides the therapeutic benefits of NSAIDs while causing a much lower incidence of side-effects than typically obsd. with such agents. Thus, prodrug II substantially reduced GI toxicity (15% that of naproxen) while maintaining efficacy in anti-inflammation activity in both acute and chronic inflammation in animal models [e.g., rat carrageenan-induced hindlimb edema, P = 0.78 ± 0.04 (4 h) and P = 0.93 ± 0.04 (5 h)].
- ST NSAID modified prepn therapeutic benefit reduced side effect; nonsteroidal antiinflammatory drug modified prepn reduced side effect; naproxen sodium modified prepn
- IT Sulfones  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (C1-10-alkyl and aryl; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
 (dispersions; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Toxicity  
 (drug, side-effect redn.; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
 (emulsions; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
 (enteric; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
 (liposomes; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
 (micelles; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Analgesics  
 Antiarthritics  
 Pharmacokinetics  
 (modification of pharmacol. active agents for use as nonsteroidal



- anti-inflammatory drugs)
- IT Anti-inflammatory agents  
(nonsteroidal; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
(prodrugs; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Digestive tract  
(reduced toxicity; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Sulfonamides  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(reverse; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Sulfonic acids, preparation  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(salts, C1-10-alkyl and aryl; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Sulfinic acids  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(salts, reverse; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
(solids; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Drug delivery systems  
(solns.; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Functional groups  
(sulfur-contg. groups; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT Digestive tract  
(ulcer, side-effect redn.; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT 329967-85-3, COX-1  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibition; modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT 354145-55-4P  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT 22204-53-1, Naproxen  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)
- IT 63-74-1, 4-Aminobenzenesulfonamide 70-55-3, p-Methylbenzenesulfonamide  
80-17-1, Benzenesulfonyl hydrazide 98-09-9, Benzenesulfonyl chloride  
98-59-9, p-Toluenesulfonyl chloride 98-68-0, p-Methoxybenzenesulfonyl chloride 98-74-8, p-Nitrobenzenesulfonyl chloride 107-15-3, Ethylenediamine, reactions 107-21-1, Ethylene glycol, reactions 110-63-4, 1,4-Butanediol, reactions 111-29-5, 1,5-Pentanediol 111-46-6, Diethylene glycol, reactions 124-63-0, Methanesulfonyl chloride 421-83-0, Trifluoromethanesulfonyl chloride 504-63-2, 1,3-Propanediol 505-10-2, 3-(Methylthio)propanol 556-48-9,

- 1,4-Cyclohexanediol 594-44-5, Ethanesulfonyl chloride 625-69-4,  
 2,4-Pentanediol 629-11-8, 1,6-Hexanediol 699-12-7,  
 2-(Phenylthio)ethanol 777-44-6, m-(Trifluoromethyl)benzenesulfonyl  
 chloride 1950-68-1, 4-Methoxybenzenesulfonyl hydrazide 2508-29-4,  
 5-Aminopentanol 2580-77-0, 2,2'-Sulfonyldiethanol 3144-09-0,  
 Methanesulfonamide 3446-90-0, 4-(Methylthio)benzyl alcohol 4048-33-3,  
 6-Aminohexanol 5271-38-5, 2-(Methylthio)ethanol 5455-59-4,  
 o-Nitrobenzenesulfonamide 5470-49-5, 4-(Methanesulfonyl)aniline  
 10210-17-0, 3-(4-Hydroxyphenyl)propanol 13325-10-5, 4-Aminobutanol  
 15205-66-0, 2-Hydroxyethyl methyl sulfone 20582-85-8 35303-76-5,  
 4-(2-Aminoethyl)benzenesulfonamide 41687-30-3, 2-Hydroxyethyl  
 m-nitrophenyl sulfone 78521-69-4, N-(4-Hydroxybutyl)toluenesulfonamide  
 78894-78-7, 2-Aminoethanol tosylate 385369-59-5, 2-Aminoethanol mesylate  
 385369-67-5, [(Methanesulfonyl)methyl]amine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (modification of pharmacol. active agents for use as nonsteroidal  
 anti-inflammatory drugs)
- IT 16780-44-2P, 5-(Tosylamino)pentanol 87426-50-4P, Naproxen 2-hydroxyethyl  
 ester 106996-61-6P 120339-20-0P, Diclofenac 3-hydroxypropyl ester  
 126962-41-2P, Ibuprofen 3-hydroxypropyl ester 156967-30-5P, Naproxen  
 3-hydroxypropyl ester 156967-31-6P, Naproxen 6-hydroxyhexyl ester  
 184474-04-2P, Naproxen 4-hydroxybutyl ester 214708-31-3P, Ketoprofen  
 3-hydroxypropyl ester 354145-60-1P, Indomethacin 3-hydroxypropyl ester  
 385369-36-8P 385369-62-0P 385369-83-5P, 6-(Tosylamino)hexanol  
 385369-91-5P, N-(4-Hydroxybutyl)methanesulfonamide 385369-92-6P,  
 3-(4-Hydroxyphenyl)propanol ditosylate 385424-07-7P 385800-13-5P,  
 Naproxen 5-hydroxypentyl ester 385800-14-6P, Flurbiprofen  
 3-hydroxypropyl ester 385800-15-7P, Carprofen 3-hydroxypropyl ester  
 385800-17-9P, Naproxen 2-(methylthio)ethyl ester 385800-18-0P, Naproxen  
 3-(methylthio)propyl ester 385800-19-1P, Naproxen 4-(methylthio)butyl  
 ester 385800-20-4P, Naproxen 2-(phenylthio)ethyl ester 385800-24-8P,  
 Naproxen 4-(methylthio)benzyl ester  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (modification of pharmacol. active agents for use as nonsteroidal  
 anti-inflammatory drugs)
- IT 385369-40-4P 385369-44-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
 USES (Uses)  
 (modification of pharmacol. active agents for use as nonsteroidal  
 anti-inflammatory drugs)
- IT 53-86-1, Indomethacin 1120-71-4, Propanesultone 1633-83-6,  
 Butanesultone 5104-49-4, Flurbiprofen 15307-79-6, Diclofenac sodium  
 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen  
 26159-34-2, Naproxen sodium 53716-49-7, Carprofen  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT  
 (Reactant or reagent); USES (Uses)  
 (modification of pharmacol. active agents for use as nonsteroidal  
 anti-inflammatory drugs)
- IT 50-78-2DP, Aspirin, modified prodrug 54-21-7DP, Sodium salicylate,  
 modified prodrug 61-68-7DP, Mefenamic acid, modified prodrug  
 103-90-2DP, Acetaminophen, modified prodrug 552-94-3DP, Salsalate,  
 modified prodrug 2016-36-6DP, Choline salicylate, modified prodrug,  
 preparation 6385-02-0DP, Meclofenamate sodium, modified prodrug  
 18917-89-0DP, Magnesium salicylate, modified prodrug 21256-18-8DP,  
 Oxaprozin, modified prodrug 22494-42-4DP, Diflunisal, modified prodrug  
 23187-87-3DP, Choline magnesium salicylate, modified prodrug  
 26171-23-3DP, Tolmetin, modified prodrug 31842-01-0DP, Indoprofen,  
 modified prodrug 33005-95-7DP, Tiaprofenic acid, modified prodrug  
 34597-40-5DP, modified prodrug 36322-90-4DP, Piroxicam, modified prodrug  
 38194-50-2DP, Sulindac, modified prodrug 41340-25-4DP, Etodolac,  
 modified prodrug 42924-53-8DP, Nabumetone, modified prodrug

51803-78-2DP, Nimesulide, modified prodrug 70374-39-9DP, Lornoxicam, modified prodrug 71125-38-7DP, Meloxicam, modified prodrug 74103-07-4DP, Ketorolac tromethamine, modified prodrug 80937-31-1DP, Flosulide, modified prodrug 354145-61-2P 385369-37-9P 385369-42-6P 385369-45-9P 385369-47-1P 385369-48-2P 385369-49-3P 385369-50-6P 385369-51-7P 385369-52-8P 385369-53-9P 385369-54-0P 385369-55-1P 385369-56-2P 385369-57-3P 385369-58-4P 385369-60-8P 385369-61-9P 385369-63-1P 385369-64-2P 385369-65-3P 385369-66-4P 385369-68-6P 385369-69-7P 385369-70-0P **385369-71-1P** 385369-72-2P 385369-73-3P 385369-74-4P 385369-75-5P 385369-76-6P 385369-77-7P 385369-78-8P 385369-79-9P 385369-80-2P 385369-81-3P 385369-82-4P 385369-84-6P 385369-86-8P 385369-88-0P 385369-90-4P 385369-93-7P 385424-08-8P 385800-16-8P, Naproxen 2-(methanesulfonyl)ethyl ester 385800-21-5P, Naproxen 3-(methanesulfonyl)propyl ester 385800-22-6P, Naproxen 4-(methanesulfonyl)butyl ester 385800-23-7P, Naproxen 2-(benzenesulfonyl)ethyl ester 385800-25-9P, Naproxen 4-(methanesulfonyl)benzyl ester 385800-26-0P, Diclofenac 2-(methanesulfonyl)ethyl ester 385800-27-1P, Diclofenac 4-[(methanesulfonyl)amino]butyl ester 385800-28-2P, Diclofenac 4-[(toluenesulfonyl)amino]butyl ester

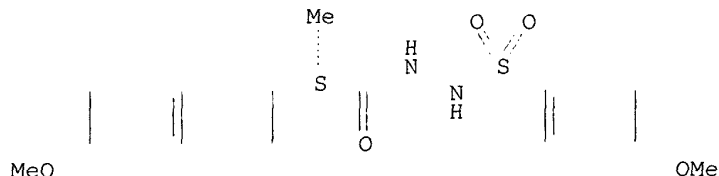
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)

IT **385369-71-1P**  
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(modification of pharmacol. active agents for use as nonsteroidal anti-inflammatory drugs)

RN 385369-71-1 HCAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy-.alpha.-methyl-, 2-[(4-methoxyphenyl)sulfonyl]hydrazide, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

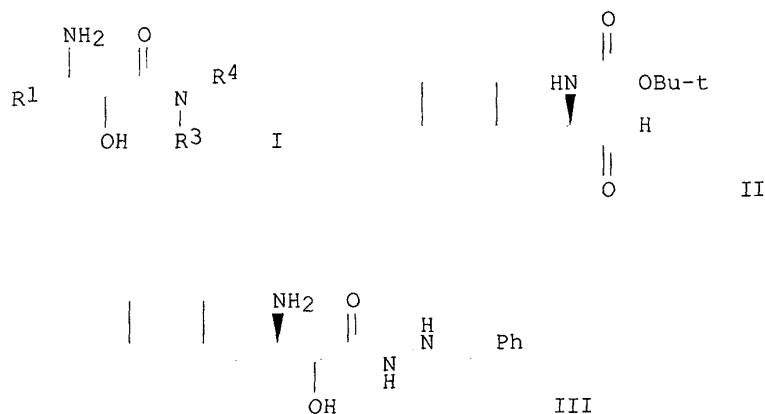


L48 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
AN 2001:780840 HCAPLUS  
DN 135:331197  
TI Synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors  
IN Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.; Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe Y.  
PA Abbott Laboratories, USA  
SO PCT Int. Appl., 1/3 pp.  
CODEN: PIXXD2  
DT **Patent**  
LA English  
IC ICM C07C243-28  
ICS C07C239-20; C07C321-14; C07D215-46; C07D213-75; C07D237-20; A61K031-165; A61K031-175; A61K031-18; A61K031-435; A61K031-50  
CC 23-18 (Aliphatic Compounds)  
Section cross-reference(s): 25, 34  
FAN.CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE

```

-----
PI  WO 2001079157      A1  20011025      WO 2001-US12274  20010413
      W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
        HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
        LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
        RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
        YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
      RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
        DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
        BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      EP 1272456      A1  20030108      EP 2001-925029  20010413
      R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-549995      A  20000414
      US 2001-813008      A  20010321
      WO 2001-US12274      W  20010413
OS   MARPAT 135:331197
GI

```



AB Title compds. I [R<sup>1</sup> = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R<sup>5</sup>S-alkylene; R<sup>3</sup> = H, alkyl, arylalkyl; R<sup>4</sup> = NR<sup>6</sup>R<sup>7</sup>, OR<sup>8</sup>; R<sup>5</sup> = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R<sup>6-7</sup> = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxyalkonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R<sup>6-7</sup> together are arylalkylidene; or R<sup>6-7</sup> together with the nitrogen atom to which they are attached, form a heterocycle; R<sup>8</sup> = H, alkanoylalkyl, alkenyl, alkoxyalkonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R<sup>9-10</sup> = H, alkyl, aryl] were prep'd. Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0.degree.C, room temp. 1 h) and oxidized to II (DMSO, Py.bul.SO<sub>3</sub>, Et<sub>3</sub>N, room temp. 30 min). II was converted to the bisulfite addn. product (H<sub>2</sub>O, NaHSO<sub>3</sub>, 5.degree.C, 24 h) and reacted with KCN to give the .alpha.-hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBT). Selected compds. I had IC<sub>50</sub> < 0.1 .mu.M for MetAP2. I are useful for inhibiting angiogenesis.

ST hydrazide alkoxyamide angiogenesis inhibitors metap2 prepn

IT Angiogenesis inhibitors

(synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)				
IT	369355-67-9P	369355-68-0P	369355-69-1P	369355-70-4P 369355-71-5P
	369355-72-6P	369355-73-7P	369355-74-8P	<b>369355-75-9P</b>
	369355-76-0P	369355-77-1P	369355-78-2P	369355-79-3P 369355-80-6P
	369355-81-7P	369355-82-8P	369355-83-9P	369355-84-0P 369355-85-1P
	369355-86-2P	369355-87-3P	369355-88-4P	369355-89-5P 369355-90-8P
	369355-91-9P	369355-92-0P	369355-93-1P	369355-94-2P 369355-95-3P
	369355-96-4P	369355-97-5P	369355-98-6P	369355-99-7P 369356-00-3P
	369356-01-4P	369356-02-5P	369356-03-6P	369356-04-7P 369356-05-8P
	369356-06-9P	369356-07-0P	369356-08-1P	369356-09-2P 369356-10-5P
	369356-11-6P	369356-12-7P	369356-13-8P	369356-14-9P 369356-15-0P
	369356-16-1P	369356-17-2P	369356-18-3P	369356-19-4P 369356-20-7P
	369356-21-8P	369356-22-9P	369356-23-0P	369356-24-1P 369356-25-2P
	369356-26-3P	369356-27-4P	369356-28-5P	369356-29-6P 369356-30-9P
	369356-31-0P	369356-32-1P	369356-33-2P	369356-34-3P 369356-35-4P
	369356-36-5P	369356-37-6P	369356-38-7P	369356-39-8P 369356-40-1P
	369356-41-2P	369356-42-3P	369356-43-4P	369356-44-5P 369356-45-6P
	369356-46-7P	369356-47-8P	369356-48-9P	369356-49-0P 369356-50-3P
	369356-51-4P	369356-52-5P	369356-53-6P	369356-54-7P 369356-55-8P
	369356-56-9P	369356-57-0P	369356-58-1P	369356-59-2P 369356-60-5P
	369356-61-6P	369356-62-7P	369356-63-8P	369356-64-9P 369356-65-0P
	369356-66-1P	369356-67-2P	369356-68-3P	369356-69-4P 369356-70-7P
	369356-71-8P	369356-72-9P	369356-73-0P	369356-74-1P 369356-75-2P
	369356-76-3P	369356-77-4P	369356-78-5P	369356-79-6P 369356-80-9P
	369356-81-0P	369356-82-1P	369356-83-2P	369356-84-3P 369356-85-4P
	369356-86-5P	369356-87-6P	369356-88-7P	369356-89-8P 369356-90-1P
	369356-91-2P	369356-92-3P	369356-93-4P	369356-94-5P 369356-95-6P
	369356-96-7P	369356-97-8P	369356-98-9P	369356-99-0P 369357-00-6P
	369357-01-7P	369357-02-8P	369357-03-9P	369357-04-0P 369357-05-1P
	369357-06-2P	369357-07-3P	369357-08-4P	369357-09-5P 369357-10-8P
	369357-11-9P	369357-12-0P	369357-13-1P	369357-14-2P 369357-15-3P
	369357-16-4P	369357-17-5P	369357-18-6P	369357-19-7P 369357-20-0P
	369357-21-1P	369357-22-2P	369357-23-3P	369357-24-4P 369357-25-5P
	369357-26-6P	369357-27-7P	369357-28-8P	369357-29-9P 369357-30-2P
	369357-32-4P	369357-34-6P	369357-36-8P	369357-38-0P 369357-40-4P
	369357-42-6P	369357-44-8P	369357-46-0P	369357-48-2P 369357-50-6P
	369357-51-7P	369357-52-8P	369357-53-9P	369357-54-0P 369357-56-2P
	369357-58-4P	369357-60-8P	369357-62-0P	369357-64-2P 369357-66-4P
	369357-68-6P	369357-69-7P	369357-70-0P	369357-71-1P 369357-72-2P
	369357-73-3P	369357-74-4P	369357-75-5P	369357-76-6P 369357-77-7P
	369357-78-8P	369357-79-9P	369357-80-2P	369357-81-3P 369357-82-4P
	369357-83-5P	369357-84-6P	369357-85-7P	369357-86-8P 369357-87-9P
	369357-88-0P	369357-89-1P	369357-90-4P	369357-91-5P 369357-92-6P
	369357-93-7P	369357-94-8P	369357-95-9P	369357-96-0P 369357-97-1P
	369357-98-2P	369357-99-3P	369358-00-9P	369358-01-0P 369358-02-1P
	369358-03-2P	369358-04-3P	369358-05-4P	369358-06-5P 369358-07-6P
	369358-08-7P	369358-09-8P	369358-10-1P	369358-11-2P 369358-12-3P
	369358-13-4P	369358-14-5P	369358-15-6P	369358-16-7P 369358-17-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)				
IT	369358-18-9P	369358-19-0P	369358-20-3P	369358-21-4P 369358-22-5P
	369358-23-6P	369358-24-7P	369358-25-8P	369358-26-9P 369358-27-0P
	369358-28-1P	369358-29-2P	369358-30-5P	369358-31-6P 369358-32-7P
	369358-33-8P	369358-34-9P	369358-35-0P	369358-37-2P 369358-38-3P
	369358-40-7P	369358-41-8P	369358-42-9P	369358-43-0P 369358-44-1P
	369358-45-2P	369358-46-3P	369358-48-5P	369358-50-9P 369358-52-1P
	369358-53-2P	369358-54-3P	369358-55-4P	369358-57-6P 369358-59-8P
	369358-60-1P	369358-61-2P	369358-62-3P	369358-63-4P 369358-64-5P
	369358-65-6P	369358-66-7P	369358-67-8P	369358-68-9P 369358-69-0P

369358-70-3P	369358-71-4P	369358-72-5P	369358-73-6P	369358-74-7P
369358-75-8P	369358-76-9P	369358-77-0P	369358-78-1P	369358-79-2P
369358-80-5P	369358-81-6P	369358-82-7P	369358-83-8P	369358-84-9P
369358-85-0P	369358-86-1P	369358-87-2P	369358-88-3P	369358-89-4P
369358-90-7P	369358-91-8P	369358-92-9P	369358-93-0P	369358-94-1P
369358-95-2P	369358-96-3P	369358-97-4P	369358-98-5P	369358-99-6P
369359-00-2P	369359-01-3P	369359-02-4P	369359-03-5P	369359-04-6P
369359-05-7P	369359-06-8P	369359-07-9P	369359-08-0P	369359-09-1P
369359-10-4P	369359-11-5P	369359-12-6P	369359-13-7P	369359-14-8P
369359-15-9P	369359-16-0P	369359-17-1P	369359-18-2P	369359-19-3P
369359-20-6P	369359-21-7P	369359-22-8P	369359-23-9P	369359-24-0P
369359-25-1P	369359-26-2P	369359-27-3P	369359-28-4P	369359-29-5P
369359-30-8P	369359-31-9P	369359-32-0P	369359-33-1P	369359-34-2P
369359-35-3P	369359-36-4P	369359-37-5P	369359-38-6P	369359-39-7P
369359-40-0P	369359-41-1P	369359-42-2P	369359-43-3P	369359-44-4P
369359-45-5P	369359-46-6P	369359-47-7P	369359-48-8P	369359-49-9P
<b>369359-50-2P</b>	369359-51-3P	369359-52-4P	369359-53-5P	
369359-55-7P	369359-56-8P	369359-57-9P	369359-58-0P	369359-59-1P
369359-60-4P	369359-61-5P	369359-62-6P	369359-63-7P	369359-64-8P
369359-65-9P	369359-66-0P	369359-67-1P	369359-68-2P	369359-69-3P
369359-71-7P	369359-72-8P	369359-73-9P	369359-74-0P	369359-75-1P
369359-76-2P	369359-77-3P	369359-78-4P	369359-79-5P	369359-80-8P
369359-81-9P	369359-82-0P	369359-83-1P	369359-84-2P	369359-85-3P
369359-86-4P	369359-87-5P	369359-88-6P	369359-89-7P	369359-90-0P
369359-91-1P	369359-92-2P	369359-93-3P	369359-94-4P	369359-95-5P
369359-96-6P	369359-97-7P	369359-98-8P	369359-99-9P	369360-00-9P
369360-01-0P	369360-02-1P	369360-03-2P	369360-04-3P	369360-05-4P
369360-06-5P	369360-07-6P	369360-08-7P	369360-09-8P	369360-10-1P
369360-11-2P	369360-12-3P	369360-13-4P	369360-14-5P	369360-15-6P
369360-16-7P	369360-17-8P	369360-18-9P	369360-19-0P	369360-20-3P
369360-21-4P	369360-22-5P	369360-23-6P	369360-24-7P	369360-25-8P
369360-26-9P	369360-27-0P	369360-28-1P	369360-29-2P	369360-30-5P
369360-31-6P	369360-32-7P	369360-33-8P	369360-34-9P	369360-35-0P
369360-36-1P	369360-37-2P	369360-38-3P	369360-39-4P	369360-40-7P
369360-41-8P	369360-42-9P	369360-43-0P	369360-44-1P	369360-45-2P
369360-46-3P	369360-47-4P	369360-48-5P		

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)

IT 585-71-7P 18328-11-5P, Benzenebutanal 39684-80-5P,  
N-(tert-Butoxycarbonyl)-2-bromoethylamine 52245-11-1P 58634-67-6P  
67032-33-1P, Methyl 3-(2,3-dihydroxypropyloxy)benzoate 68432-92-8P,  
Methyl 3-(cyanomethyl)benzoate 71925-14-9P 79250-46-7P, Methyl  
3-(prop-2-enyloxy)benzoate 110238-61-4P 129593-17-5P 148433-10-7P,  
Methyl 3-propoxybenzoate 160820-17-7P 172789-09-2P 339592-56-2P  
360788-02-9P, 3-(3-Indolyl)propanal 369360-49-6P 369360-50-9P  
369360-51-0P 369360-52-1P 369360-53-2P 369360-54-3P 369360-55-4P  
369360-56-5P 369360-57-6P 369360-58-7P 369360-59-8P 369360-60-1P  
369360-61-2P 369360-62-3P 369360-63-4P 369360-64-5P 369360-65-6P  
369360-66-7P 369360-67-8P 369360-68-9P 369360-69-0P 369360-70-3P  
369360-71-4P 369360-72-5P, Ethyl 4-ethyloct-2-enoate 369360-73-6P  
369360-74-7P 369360-75-8P 369360-76-9P 369360-77-0P 369360-78-1P  
369360-79-2P 369360-80-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis inhibitors)

IT 50-45-3, 2,3-Dichlorobenzoic acid 50-79-3, 2,5-Dichlorobenzoic acid  
50-84-0, 2,4-Dichlorobenzoic acid 51-36-5, 3,5-Dichlorobenzoic acid  
51-44-5, 3,4-Dichlorobenzoic acid 51-71-8, 1-(2-Phenethyl)hydrazine  
55-22-1, 4-Pyridinecarboxylic acid, reactions 64-04-0,

2-Phenylethylamine 69-72-7, 2-Hydroxybenzoic acid, reactions 74-11-3,  
4-Chlorobenzoic acid 75-26-3, 2-Bromopropane 78-77-3,  
1-Bromo-2-methylpropane 79-31-2, 2-Methylpropionic acid 86-55-5,  
1-Naphthoic acid 86-87-3, 1-Naphthylacetic acid 88-13-1,  
3-Thiophenecarboxylic acid 88-14-2, Furan-2-carboxylic acid 88-65-3,  
2-Bromobenzoic acid 91-40-7, N-Phenylanthranilic acid 91-52-1,  
2,4-Dimethoxybenzoic acid 93-07-2, 3,4-Dimethoxybenzoic acid 93-25-4,  
2-Methoxyphenylacetic acid 94-53-1, 1,3-Benzodioxole-5-carboxylic acid  
98-73-7, 4-tert-Butylbenzoic acid 98-85-1 98-89-5,  
Cyclohexanecarboxylic acid 98-97-5, 2-Pyrazine carboxylic acid  
98-98-6, 2-Pyridinecarboxylic acid 99-04-7, 3-Methylbenzoic acid  
99-05-8, 3-Aminobenzoic acid 99-06-9, 3-Hydroxybenzoic acid, reactions  
99-64-9, 3-Dimethylaminobenzoic acid 99-94-5, 4-Methylbenzoic acid  
99-96-7, 4-Hydroxybenzoic acid, reactions 100-09-4, 4-Methoxybenzoic  
acid 100-63-0, 1-Phenylhydrazine 103-82-2, Phenylacetic acid,  
reactions 104-01-8, 4-Methoxyphenylacetic acid 104-88-1,  
4-Chlorobenzaldehyde, reactions 106-94-5, 1-Bromopropane 111-14-8,  
Heptanoic acid 118-41-2, 3,4,5-Trimethoxybenzoic acid, reactions  
118-90-1, 2-Methylbenzoic acid 118-91-2, o-Chlorobenzoic acid  
118-92-3, 2-Aminobenzoic acid 134-11-2, 2-Ethoxybenzoic acid 150-13-0,  
4-Aminobenzoic acid 349-46-2, D-Cystine 368-78-5 368-90-1,  
1-[4-(Trifluoromethyl)phenyl]hydrazine 371-14-2, 1-(4-  
Fluorophenyl)hydrazine 445-29-4, 2-Fluorobenzoic acid 454-92-2,  
3-(Trifluoromethyl)benzoic acid 455-24-3, 4-(Trifluoromethyl)benzoic  
acid 455-38-9, 3-Fluorobenzoic acid 456-22-4, 4-Fluorobenzoic acid  
488-93-7, Furan-3-carboxylic acid 499-06-9, 3,5-Dimethylbenzoic acid  
501-81-5, 3-Pyridylacetic acid 503-74-2, 3-Methylbutyric acid  
524-38-9, N-Hydroxyphthalamide 527-72-0, 2-Thiophenecarboxylic acid  
530-50-7 536-40-3, 4-Chlorobenzohydrazide 536-66-3, 4-Isopropylbenzoic  
acid 537-47-3, N-Phenylhydrazinecarboxamide 539-44-6,  
1-(4-Methylphenyl)hydrazine 556-08-1, 4-Acetamidobenzoic acid  
579-75-9, o-Anisic acid 581-96-4, 2-Naphthylacetic acid 585-76-2,  
3-Bromobenzoic acid 586-38-9, 3-Methoxybenzoic acid 586-76-5,  
4-Bromobenzoic acid 589-21-9, 1-(4-Bromophenyl)hydrazine 593-56-6,  
O-Methylhydroxylamine hydrochloride 603-79-2, 2,3-Dimethylbenzoic acid  
610-72-0, 2,5-Dimethylbenzoic acid 611-01-8, 2,4-Dimethylbenzoic acid  
612-35-1, .alpha.-Phenyl-o-toluic acid 613-94-5, Benzohydrazide  
615-21-4 618-40-6, 1-Methyl-1-phenylhydrazine 619-04-5,  
3,4-Dimethylbenzoic acid 619-64-7, 4-Ethylbenzoic acid 619-65-8,  
4-Cyanobenzoic acid 619-84-1, 4-Dimethylaminobenzoic acid 619-86-3,  
4-Ethoxybenzoic acid 622-36-6, 1-(2-Methylphenyl)hydrazine 634-97-9,  
2-Pyrrole carboxylic acid 636-10-2, 1-(3-Methylbutyl)-1-phenylhydrazine  
636-44-2, 2,5-Dimethyl-3-furoic acid 636-97-5, 4-Nitrobenzohydrazide  
637-80-9, Ethyl hydrazinoacetate 644-21-3, 1-Ethyl-1-phenylhydrazine  
658-27-5, 1-(3-Fluorophenyl)hydrazine 699-90-1, 3-Fluoro-2-methylbenzoic  
acid 771-61-9, Pentafluorophenol 825-99-0, 3-(Methylthio)benzoic acid  
830-96-6, 1H-Indole-3-propanoic acid 867-13-0, Triethyl phosphonoacetate  
870-46-2, tert-Butyl hydrazinecarboxylate 1014-81-9,  
3-(Trifluoromethoxy)benzoic acid 1073-69-4, 1-(4-Chlorophenyl)hydrazine  
1115-59-9, L-Alanine ethyl ester hydrochloride 1123-00-8,  
Cyclopentylacetic acid 1129-28-8, Methyl 3-(bromomethyl)benzoate  
1132-21-4, 3,5-Dimethoxybenzoic acid 1438-16-0, 3-Amino-2-thioxo-1,3-  
thiazolidin-4-one 1452-63-7 1498-96-0, 4-Butoxybenzoic acid  
1521-38-6, 2,3-Dimethoxybenzoic acid 1538-08-5 1576-35-8,  
4-Methylphenylsulfonylhydrazine 1621-91-6, 1H-Pyrazole-5-carboxylic acid  
1673-47-8, 3-Chlorobenzohydrazide 1798-09-0, 3-Methoxyphenylacetic acid  
1821-12-1, 4-Phenylbutyric acid 1877-72-1, 3-Cyanobenzoic acid  
1878-65-5, 3-Chlorophenylacetic acid 1878-66-6, 4-Chlorophenylacetic  
acid 1918-79-2, 5-Methylthiophene-2-carboxylic acid 2164-61-6,  
3-Pyridazine carboxylic acid 2213-43-6, 1-Aminopiperidine 2215-77-2,  
4-Phenoxybenzoic acid 2243-55-2, 1-Naphthylhydrazine 2361-27-5,  
2-Thiophenecarbohydrazide 2368-80-1, 1-(2-Fluorophenyl)hydrazine  
2438-05-3, 4-n-Propylbenzoic acid 2444-36-2, 2-Chlorophenylacetic acid

2550-36-9, (Bromomethyl)cyclohexane 2576-47-8, 2-Bromoethylamine  
hydrobromide 2687-43-6, O-Benzylhydroxylamine hydrochloride 2785-98-0,  
2,5-Dimethoxybenzoic acid 3235-69-6, 4-Morpholineacetic acid  
3332-29-4, O-Ethylhydroxylamine hydrochloride 3400-45-1,  
Cyclopentanecarboxylic acid 3438-16-2, 5-Chloro-2-methoxybenzoic acid  
3471-32-7, 1-(4-Methoxyphenyl)hydrazine 3619-22-5, 4-  
Methylbenzohydrazide 3839-22-3, 2-Cyanobenzoic acid 3919-73-1,  
O-(Carboethoxy)methylhydroxylamine hydrochloride 3973-08-8, 4-Thiazole  
carboxylic acid 4052-30-6, 4-(Methylsulfonyl)benzoic acid 4361-28-8,  
3-Cyclohexylpropanal 4392-54-5, 4-Hydrazinobenzenesulfonamide  
4519-39-5, 2,3-Difluorobenzoic acid 4761-00-6, 2,4,6-Trimethylbenzyl  
bromide 4846-21-3, O-Phenylhydroxylamine 4890-85-1,  
2-Bibenzylcarboxylic acid 4930-98-7, 2-Hydrazinopyridine 5042-30-8,  
1-(2,2,2-Trifluoroethyl)hydrazine 5292-21-7, Cyclohexylacetic acid  
5331-43-1, Benzyl carbazate 5341-58-2, 3-Hydroxy-2-naphthoylhydrazine  
5409-31-4, 3,4-Diethoxybenzoic acid 5429-28-7, 4-(Diethylamino)benzoic  
acid 5438-19-7, 4-Propoxybenzoic acid 5537-74-6, 3-(Ethylthio)benzoic  
acid 5728-52-9, 4-Phenylphenylacetic acid 5785-06-8,  
3-Methoxybenzohydrazide 5814-05-1, 2-Chlorobenzohydrazide 5818-06-4,  
3-Hydroxybenzoyl hydrazide 6027-14-1, D-Homocysteine 6084-58-8,  
O-Isobutylhydroxylamine hydrochloride 6092-80-4, O-Phenylhydroxylamine  
hydrochloride 6498-34-6, 1-Cyclohexylhydrazine 6638-79-5,  
N,O-Dimethylhydroxylamine hydrochloride 6688-11-5, Cyclooctanaldehyde  
6973-60-0, 1-Methylpyrrole-2-carboxylic acid 7466-54-8,  
2-Methoxybenzohydrazide 10449-07-7, 1-(2-Chlorophenyl)hydrazine  
13050-47-0, 3-Methylbenzohydrazide 13115-43-0, 2-Pyridylacetic acid  
13116-27-3, 1-(4-Iodophenyl)hydrazine 13205-46-4, 4-Isopropoxybenzoic  
acid 13205-48-6, 4-Methylthiobenzoic acid 13205-49-7,  
4-(Ethylthio)benzoic acid 13205-50-0, 4-(Isopropylthio)benzoic acid  
13221-86-8, 2,4-Dihydroxybenzohydrazide 13636-54-9, 1-Mesitylhydrazine  
13957-54-5 14190-59-1, 2-Thiazole carboxylic acid 14527-41-4,  
5-Thiazolecarboxylic acid 14763-20-3, 1-(3-Chlorophenyl)hydrazine  
15384-39-1, 1-(3-Methoxyphenyl)hydrazine 16182-15-3 16596-41-1,  
1-Pyrrolidinamine 16874-33-2, 2-Tetrahydrofuroic acid 17078-28-3,  
4-Dimethylaminophenylacetic acid 17284-97-8, 3-Chloro-6-  
hydrazinopyridazine 17894-25-6, 2,5-Dimethoxybenzohydrazide 19275-55-9  
19438-10-9, Methyl 3-hydroxybenzoate 20570-96-1 21169-71-1,  
5-Isoxazolecarboxylic acid 22026-39-7 22683-48-3, 4-  
(Propylthio)benzoic acid 22683-49-4, 4-(Butylthio)benzoic acid  
22683-51-8, 4-(Hexylthio)benzoic acid 22855-95-4, 4-(Benzylthio)benzoic  
acid 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23834-14-2,  
7-Chloro-4-hydrazinoquinoline 25503-90-6, 1-Acetylpiperidine-4-  
carboxylic acid 28356-58-3, 4-Pyridylacetic acid 30923-92-3,  
1-(Cyclopentyl)hydrazine 30963-12-3, 2-(1-Methylhydrazino)-3-  
nitropyridine 31462-59-6, 4-Pyrimidine carboxylic acid 31719-76-3,  
4-(Phenoxymethyl)benzoic acid 32443-99-5, D-Cysteine hydrochloride  
32910-52-4, 4-(Cyclohexylthio)benzoic acid 32910-56-8,  
4-(4-Methylpentylthio)benzoic acid 32910-70-6, 4-(2-  
Cyclohexylethylthio)benzoic acid 36239-09-5, Ethyl-3-chloro-3-oxo  
propionate 36331-57-4, Benzylsulfonylhydrazine 37718-11-9,  
1H-Pyrazole-4-carboxylic acid 37860-70-1, 2,3-Diethoxybenzoic acid  
38945-21-0, O-Allylhydroxylamine hydrochloride 39115-96-3,  
3-Bromobenzohydrazide 39627-84-4, 2-Naphthoylhydrazine 39684-28-1,  
O-tert-Butylhydroxylamine hydrochloride 39943-56-1, 1-(3,5-  
Dichlorophenyl)hydrazine 40594-30-7, 1-(2,4-Difluorophenyl)hydrazine  
40887-80-7, 1-(3-Bromophenyl)hydrazine 43038-45-5, 1-Naphthoylhydrazine  
46230-31-3, O-(Carbobenzoyloxy)methylhydroxylamine 51304-65-5,  
1-(3-Chloro-4-methylphenyl)hydrazine 51421-13-7, 1-(2-  
Chlorobenzyl)hydrazine 51546-12-4, 2-Chloro-5-(methylthio)benzoic acid  
51707-38-1, 3,5-Dimethoxybenzohydrazide 53516-97-5, 3-  
Chlorophenylsulfonylhydrazine 53551-35-2, 4-(2-Methylpropylthio)benzoic  
acid 54699-92-2 58586-81-5, 4-Ethoxybenzohydrazide 58791-94-9,  
1-(4-Chloro-2-methylphenyl)hydrazine 59983-39-0, (2S)-2-(Methoxymethyl)-



1-pyrrolidinamine 60739-40-4, 3-(Benzylthio)benzoic acid 61645-34-9,  
2-Hydrazinoquinoxaline 61715-74-0, 1-Propyl-1-phenylhydrazine  
62524-21-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
inhibitors)

IT 63693-65-2, 1-(4-Isopropylphenyl)hydrazine 65227-54-5,  
1-Naphthylsulfonylhydrazine 66971-55-9, 5-Hydrazino-1,3-dimethyl-4-nitro-  
1H-pyrazole 67487-35-8, 2,5-Dichlorobenzohydrazide 70491-05-3,  
(2R)-2-[(tert-Butoxycarbonyl)amino]-2-(cyclohexyl)ethanoic acid  
71056-18-3, 1-(Cyclopropylmethyl)-1-phenylhydrazine 72748-99-3,  
(2R)-2-(Methoxymethyl)-1-pyrrolidinamine 73469-90-6 75681-13-9, Methyl  
3-hydrazino-2-thiophenecarboxylate 76953-33-8, 3-Chloro-6-(1-  
methylhydrazino)pyridazine 79786-62-2, 1-Octyl-1-phenylhydrazine  
82732-07-8, (2R)-2-[(tert-Butoxycarbonyl)amino]-4-phenylbutanoic acid  
83823-06-7, 6-Chloro(2H)-1-benzopyran-3-carboxylic acid 84282-78-0,  
3-Chloro-4-fluorophenylhydrazine 88561-15-3, 1-Hexyl-1-phenylhydrazine  
89364-31-8 96017-23-1, 4-Chloro-2-methyl-5-(1-methylhydrazino)-3(2H)-  
pyridazinone 97108-50-4, 1-(2,5-Difluorophenyl)hydrazine 104636-55-7,  
1-(3-Phenylpropyl)-1-phenylhydrazine 106087-14-3, 1-(2-Methylpropyl)-1-  
phenylhydrazine 108329-74-4, (2R)-2-[(tert-Butoxycarbonyl)amino]-4-  
(ethylthio)butanoic acid 110208-00-9, 3-(Propylthio)benzoic acid  
114670-74-5 114838-12-9, 3-(Isopropylthio)benzoic acid 127095-92-5,  
(2R)-2-[(tert-Butoxycarbonyl)amino]-3-cyclohexylpropanoic acid  
140853-10-7 163620-24-4, 2-(1-Methylhydrazino)-5-  
(trifluoromethyl)pyridine 170162-56-8, 3-(Butylthio)benzoic acid  
172516-47-1 175137-28-7, Methyl 2-hydrazino-4-(trifluoromethyl)-5-  
pyrimidinecarboxylate 175137-33-4 175276-74-1, 1-(2-Chloro-6-  
fluorophenyl)hydrazine 207974-22-9, N-(4-Chloro-2-  
methoxyphenyl)hydrazinecarboxamide 240407-62-9 369360-81-6  
369360-82-7 369360-83-8 369360-84-9, 1-Pentyl-1-phenylhydrazine  
369360-85-0, 1-(2-Methylbutyl)-1-phenylhydrazine 369360-86-1,  
1-(2-Methylpentyl)-1-phenylhydrazine 369360-87-2, 1-(3-Methylpentyl)-1-  
phenylhydrazine 369360-88-3, 1-(3,3-Dimethylbutyl)-1-phenylhydrazine  
369360-89-4, 1-(2-Ethylbutyl)-1-phenylhydrazine 369360-90-7,  
1-Dodecyl-1-phenylhydrazine 369360-91-8, 1-(3,5,5-Trimethylhexyl)-1-  
phenylhydrazine 369360-92-9, 1-(2-Benzyloxyethyl)-1-phenylhydrazine  
369360-93-0, 1-(2,2,5-Trichloropentyl)-1-phenylhydrazine 369360-94-1,  
1-Heptyl-1-phenylhydrazine 369360-95-2, 1-[3-(Methylthio)propyl]-1-  
phenylhydrazine 369360-96-3, 1-(Cyclopentylmethyl)-1-phenylhydrazine  
369360-97-4, 1-(5-Hydroxypentyl)-1-phenylhydrazine 369360-98-5,  
1-((2R)-2,3-Dihydroxypropyl)-1-phenylhydrazine 369360-99-6,  
1-(2,2-Dichlorohexyl)-1-phenylhydrazine 369361-00-2,  
1-(7-Methoxy-3,7-dimethyloctyl)-1-phenylhydrazine 369361-01-3,  
1-[2-(4-Methylphenyl)ethyl]-1-phenylhydrazine 369361-02-4,  
1-(2-Ethylhexyl)-1-phenylhydrazine 369361-03-5, 1-[2-(4-Chlorophenyl)-2-  
cyanoethyl]-1-phenylhydrazine 369361-04-6, 1-(2-Phenylpropyl)-1-  
phenylhydrazine 369361-05-7, 1-(Cyclooctylmethyl)-1-phenylhydrazine  
369361-06-8, 1-[(11Z)-1-Hexadecenyl]-1-phenylhydrazine 369361-07-9,  
1-Tridecyl-1-phenylhydrazine 369361-08-0, 4-(1-Phenylhydrazino)butanoic  
acid 369361-09-1, 1-((6Z)-6-Nonenyl)-1-phenylhydrazine 369361-10-4,  
1-((4Z)-4-Decenyl)-1-phenylhydrazine 369361-11-5, 1-(4-Pentenyl)-1-  
phenylhydrazine 369361-12-6, 1-(3,7-Dimethyl-6-octenyl)-1-  
phenylhydrazine 369361-13-7, 1-(4,4,4-Trifluorobutyl)-1-phenylhydrazine  
369361-14-8, 1-(3-Hydroxybutyl)-1-phenylhydrazine 369361-15-9,  
1-[2-[(3,7-Dimethyl-6-octenyl)oxy]ethyl]-1-phenylhydrazine 369361-16-0,  
1-[2-(3,3-Dimethylcyclohexyl)ethyl]-1-phenylhydrazine 369361-17-1,  
1-((4S)-6-Bromo-4-methylhexyl)-1-phenylhydrazine 369361-18-2,  
1-Cyclohexylmethyl-1-phenylhydrazine 369361-19-3, 3-(Hexylthio)benzoic  
acid 369361-20-6, 3-(2-Methylpropylthio)benzoic acid 369361-21-7,  
3-(4-Methylpentylthio)benzoic acid 369361-22-8, 3-(1-  
Methylpropylthio)benzoic acid 369361-23-9, 3-(2,2-  
Dimethylpropylthio)benzoic acid 369361-24-0, 3-(Cyclohexylthio)benzoic

acid 369361-25-1, 3-(2-Cyclohexylethylthio)benzoic acid 369361-26-2,  
 3-(2-Phenylethylthio)benzoic acid 369361-27-3, 3-(3-  
 Phenylpropylthio)benzoic acid 369361-28-4 369361-29-5,  
 4-(1-Methylpropylthio)benzoic acid 369361-30-8, 4-(2,2-  
 Dimethylpropylthio)benzoic acid 369361-31-9, 4-(2-  
 Phenylethylthio)benzoic acid 369361-32-0, 4-(3-Phenylpropylthio)benzoic  
 acid 369361-33-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
 inhibitors)

IT 61229-81-0, Methionine aminopeptidase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (type 2; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
 inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) American Cyanamid Co; WO 9942436 A 1999 HCAPLUS
- (2) Merck Patent GmbH; DE 19831710 A 2000 HCAPLUS
- (3) Zask, A; US 5977408 A 1999 HCAPLUS

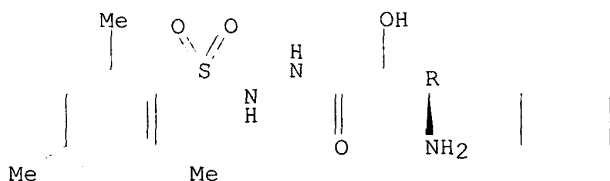
IT 369355-75-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic  
 use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug; synthesis of hydrazide and .alpha.-alkoxyamide angiogenesis  
 inhibitors)

RN 369355-75-9 HCAPLUS

CN Cyclohexanecarboxylic acid, .beta.-amino-.alpha.-hydroxy-,  
 2-[(2,4,6-trimethylphenyl)sulfonyl]hydrazide, (.beta.R)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.



L48 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:730683 HCAPLUS

DN 135:288572

TI Preparation of diphenyl ether compounds as serotonin re-uptake inhibitors

IN Andrews, Mark David; Hepworth, David; Middleton, Donald Stuart; Stobie,  
 Alan

PA Pfizer Limited, UK; Pfizer Inc.

SO PCT Int. Appl., 158 pp.

CODEN: PIXXD2

DT **Patent**

LA English

IC ICM C07C217-58

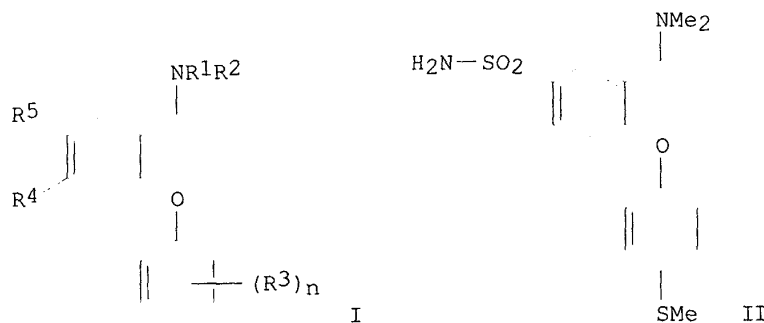
ICS C07C229-38; C07C237-28; C07C255-43; C07C255-59; C07C311-05;  
 C07C311-08; C07C311-37; C07C317-32; C07C323-20; C07C323-32;  
 C07C323-67; C07D207-12; C07D231-38; C07D233-61; C07D249-06;  
 C07D249-08; C07D295-08; C07D295-18; A61K031-137

CC 25-9 (**Benzene**, Its Derivatives, and Condensed **Benzenoid**  
 Compounds)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001072687	A1	20011004	WO 2001-IB428	20010319
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	US 2002052395	A1	20020502	US 2001-810378	20010316
	US 6448293	B2	20020910		
	EP 1268396	A1	20030102	EP 2001-917347	20010319
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
	NO 2002004663	A	20020927	NO 2002-4663	20020927
PRAI	GB 2000-7884	A	20000331		
	US 2000-197127P	P	20000414		
	WO 2001-IB428	W	20010319		
OS	MARPAT 135:288572				
GI					



AB Title compds. I [wherein R1 and R2 = independently H or (cycloalkyl)alkyl; or R1 and R2 together with the N to which they are attached form an azetidine ring; R3 = independently CF3, OCF3, alkylthio, or alkoxy; n = 1-3; R4 and R5 = independently AX; A = CH:CH or (CH2)p; p = 0-2; X = H, halo, OH, alkoxy, NO2, CN, CHO, alkylthio, alkylsulfinyl, alkylsulfonyl, or (un)substituted carbamoyl, sulfamoyl, amino, carboxy, etc.; or pharmaceutically acceptable salts, solvates, or polymorphs thereof] were prepd. as monoamine re-uptake inhibitors, particularly as selective serotonin re-uptake inhibitors. For example, 4-(methylmercapto)phenol was coupled with 2-fluorobenzaldehyde using K2CO3 in DMF to give 2-[4-(methylsulfonyl)phenoxy]benzaldehyde (100%). The aldehyde was dissolved in THF, DCM, Me2NH.bul.HCl, and TEA, treated with NaBH(OAc)3, and converted to the salt with 1M HCl in Et2O to afford N,N-dimethyl-N-[2-[4-(methylsulfonyl)phenoxy]benzyl]amine.bul.HCl (84%). Coupling the salt with ClSO3H in CH2Cl2 at 0.degree. to 5.degree.C, followed by stepwise addn. of MeCN with POCl3 and ammonia, produced the desired sulfonamide (II) in 61% yield. The latter showed serotonin re-uptake inhibition (SRI) activity with IC50 .ltoreq. 50 nM and was > 100-fold as potent in the inhibition of serotonin re-uptake than in the inhibition of dopamine and noradrenaline re-uptake. I are useful in

the treatment of disorders such as depression, attention deficit hyperactivity disorder, obsessive-compulsive disorder, post-traumatic stress disorder, substance abuse disorders, and sexual dysfunction, including premature ejaculation (no data).

ST diphenyl ether prepn serotonin reuptake inhibitor; ether diphenyl prepn antidepressant; attention deficit hyperactivity disorder treatment diphenyl ether prepn; obsessive compulsive disorder treatment diphenyl ether prepn; posttraumatic stress disorder treatment diphenyl ether prepn; substance abuse treatment diphenyl ether prepn; sexual dysfunction treatment diphenyl ether prepn

IT Drugs of abuse  
(abuse of, treatment; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Mental disorder  
(attention deficit hyperactivity disorder, treatment; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Sexual behavior  
(disorder, treatment; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Stress, animal  
(emotional, treatment of post-traumatic; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Transport proteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(monoamine-transporting, modulator; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Mental disorder  
(obsession-compulsion, treatment; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Sexual behavior  
(premature ejaculation, treatment; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT Antidepressants  
(prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT 19555-09-0P, 3-Methoxy-4-(methylsulfanyl)phenol 60789-49-3P, 1-(Methylsulfanyl)-4-nitro-2-(trifluoromethyl)benzene 63094-56-4P, 4-(Methylsulfanyl)-3-(trifluoromethyl)aniline 78940-67-7P 95920-60-8P, 5-(Allyloxy)-1,3-benzoxathiol-2-one 127087-14-3P, 4-Methoxy-3-(methylsulfanyl)phenol 170282-24-3P, 5-(Benzyloxy)-2-sulfanylphenol 170283-11-1P, 6-(Benzyloxy)-1,3-benzoxathiol-2-one 217186-17-9P 289717-37-9P 361212-81-9P 364323-56-8P 364323-57-9P 364323-58-0P 364323-59-1P 364323-60-4P 364323-61-5P 364323-62-6P 364323-63-7P 364323-64-8P 364323-65-9P 364323-66-0P 364323-67-1P 364323-68-2P 364323-69-3P 364323-71-7P 364323-72-8P 364323-73-9P 364323-74-0P 364323-75-1P 364323-76-2P 364323-77-3P 364323-78-4P 364323-79-5P 364323-80-8P 364323-81-9P 364323-82-0P 364323-83-1P 364323-84-2P 364323-85-3P 364323-86-4P 364323-87-5P 364323-88-6P 364323-89-7P 364323-90-0P 364323-91-1P 364323-92-2P 364323-93-3P 364323-95-5P 364323-96-6P 364323-97-7P 364323-98-8P 364323-99-9P 364324-00-5P 364324-01-6P 364324-02-7P 364324-03-8P 364324-04-9P 364324-05-0P 364324-06-1P 364324-07-2P 364324-08-3P 364324-09-4P 364324-10-7P 364324-11-8P 364324-12-9P 364324-13-0P 364324-14-1P 364324-15-2P 364324-16-3P 364324-17-4P 364324-18-5P 364324-19-6P 364324-20-9P 364324-22-1P 364324-23-2P 364324-24-3P 364324-25-4P 364324-26-5P 364324-27-6P 364324-28-7P 364324-29-8P **364324-30-1P** **364324-31-2P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT 364321-43-7P 364321-47-1P 364321-48-2P 364321-49-3P 364321-52-8P 364321-53-9P 364321-54-0P 364321-56-2P 364321-57-3P 364321-58-4P

364321-59-5P	364321-61-9P	364321-62-0P	364321-64-2P	364321-65-3P
364321-66-4P	364321-67-5P	364321-68-6P	364321-70-0P	364322-18-9P
364322-19-0P	364322-20-3P	364322-21-4P	364322-28-1P	364322-29-2P
364322-33-8P	364322-34-9P	364322-35-0P	364322-36-1P	364322-37-2P
364322-39-4P	364322-42-9P	364322-43-0P	364322-59-8P	364322-60-1P
364322-61-2P	364322-62-3P	364322-64-5P	364322-65-6P	364322-66-7P
364322-67-8P	364322-77-0P	364322-79-2P	364322-80-5P	364322-81-6P
364322-95-2P	364322-96-3P	364322-97-4P	364322-98-5P	364323-06-8P
364323-07-9P	364323-08-0P	364323-13-7P	364323-24-0P	364323-31-9P
364323-32-0P	364323-36-4P	364323-37-5P	364323-42-2P	364323-46-6P
364323-48-8P				

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT	364321-41-5P	364321-42-6P	364321-44-8P	364321-45-9P	364321-46-0P
	364321-50-6P	364321-51-7P	364321-55-1P	364321-71-1P	364321-72-2P
	364321-73-3P	364321-74-4P	364321-76-6P	364321-78-8P	364321-80-2P
	364321-81-3P	364321-83-5P	364321-85-7P	364321-87-9P	364321-89-1P
	364321-90-4P	364321-91-5P	364321-92-6P	364321-93-7P	364321-94-8P
	364321-95-9P	364321-96-0P	364321-97-1P	364321-98-2P	364321-99-3P
	364322-00-9P	364322-01-0P	364322-02-1P	364322-03-2P	364322-04-3P
	364322-06-5P	364322-07-6P	364322-08-7P	364322-09-8P	364322-10-1P
	364322-11-2P	364322-12-3P	364322-13-4P	364322-14-5P	364322-15-6P
	364322-16-7P	364322-17-8P	364322-22-5P	364322-23-6P	364322-24-7P
	364322-25-8P	364322-26-9P	364322-27-0P	364322-30-5P	364322-31-6P
	364322-32-7P	364322-38-3P	364322-41-8P	364322-44-1P	364322-45-2P
	364322-46-3P	364322-47-4P	364322-48-5P	364322-49-6P	364322-50-9P
	364322-51-0P	364322-52-1P	364322-53-2P	364322-54-3P	364322-55-4P
	364322-56-5P	364322-57-6P	364322-58-7P	364322-68-9P	364322-69-0P
	364322-70-3P	364322-71-4P	364322-72-5P	364322-73-6P	364322-74-7P
	364322-76-9P	364322-78-1P	364322-82-7P	364322-83-8P	364322-84-9P
	364322-85-0P	364322-86-1P	364322-87-2P	364322-88-3P	364322-89-4P
	364322-90-7P	364322-91-8P	364322-92-9P	364322-93-0P	364322-94-1P
	364322-99-6P	364323-00-2P	364323-01-3P	364323-02-4P	364323-04-6P
	364323-05-7P	364323-09-1P	364323-10-4P	364323-11-5P	364323-12-6P
	364323-14-8P	364323-15-9P	364323-16-0P	364323-17-1P	364323-18-2P
	364323-19-3P	364323-20-6P	364323-21-7P	364323-22-8P	364323-23-9P
	364323-25-1P	364323-26-2P	364323-27-3P	364323-28-4P	364323-29-5P
	364323-30-8P	364323-33-1P	364323-34-2P	364323-35-3P	364323-38-6P
	364323-39-7P	364323-40-0P	364323-41-1P	364323-43-3P	364323-45-5P
	364323-47-7P	364323-49-9P	364323-50-2P	364323-51-3P	364323-52-4P
	364323-53-5P	364323-54-6P	364323-55-7P	364324-32-3P	364324-33-4P
	364324-34-5P	364324-36-7P	364324-37-8P	364324-38-9P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(prepn. of di-Ph ether compds. as serotonin re-uptake inhibitors)

IT 79-06-1, Acrylamide, reactions 98-17-9, 3-(Trifluoromethyl)phenol 105-56-6 106-41-2, 4-Bromophenol 106-95-6, Allyl bromide, reactions 109-85-3, 2-Methoxyethylamine 110-91-8, Morpholine, reactions 288-32-4, Imidazole, reactions 288-36-8, 1H-1,2,3-Triazole 400-74-8, 2-Fluoro-5-nitrobenzotrifluoride 402-45-9, 4-(Trifluoromethyl)phenol 446-52-6, 2-Fluorobenzaldehyde 598-41-4, Glycinamide 771-61-9, Pentafluorophenol 827-99-6, 3-(Trifluoromethoxy)phenol 828-27-3, 4-(Trifluoromethoxy)phenol 1073-72-9, 4-(Methylmercapto)phenol 1820-80-0, 3-Amino-1H-pyrazole 2386-58-5, Vinylsulfonamide 2516-47-4,

Cyclopropylmethanamine 2646-90-4, 2,5-Difluorobenzaldehyde 2749-11-3,  
 (S)-2-Amino-1-propanol 2799-21-5 4991-65-5,  
 6-Hydroxy-1,3-benzoxathiol-2-one 6361-21-3, 2-Chloro-5-nitrobenzaldehyde  
 7735-56-0, 5-Hydroxy-1,3-benzoxathiol-2-one 10147-37-2, 2-Propylsulfonyl  
 chloride 16114-05-9 16588-02-6, 2-Chloro-5-nitrobenzonitrile  
 35320-23-1 36520-39-5, Azetidine hydrochloride 51517-01-2,  
 2-Methoxyethylsulfonyl chloride 57848-46-1, 4-Bromo-2-fluorobenzaldehyde  
 71924-62-4, 2-Fluoro-4,5-dimethoxybenzaldehyde 93777-26-5,  
 5-Bromo-2-fluorobenzaldehyde 105728-90-3, 2-Fluoro-5-methoxybenzaldehyde  
 112887-25-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; prepn. of di-Ph ether compds. as serotonin re-uptake  
 inhibitors)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

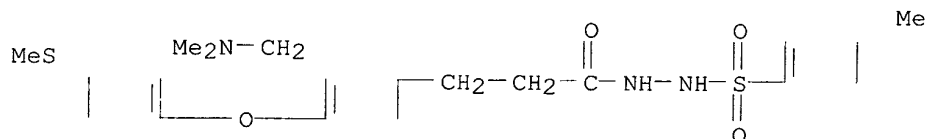
- (1) Akzo; EP 0516234 A 1992 HCAPLUS
- (2) Buckley, A; US 5334748 A 1994 HCAPLUS
- (3) Kametani, T; JOURNAL OF THE CHEMICAL SOCIETY, SECTION C: ORGANIC CHEMISTRY  
 1968, 23, P2877 HCAPLUS
- (4) Manske, R; JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 1950, V72(10), P4797
- (5) Pfizer; EP 0415613 A 1991 HCAPLUS
- (6) Pfizer Products; WO 0050380 A 2000 HCAPLUS
- (7) Yeager, G; SYNTHESIS 1995, 1, P28 HCAPLUS

IT 364324-30-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (intermediate; prepn. of di-Ph ether compds. as serotonin re-uptake  
 inhibitors)

RN 364324-30-1 HCAPLUS

CN Benzenepropanoic acid, 3-[(dimethylamino)methyl]-4-[4-(methylthio)phenoxy]-  
 , 2-[(4-methylphenyl)sulfonyl]hydrazide (9CI) (CA INDEX NAME)



L48 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:364837 HCAPLUS

DN 133:135059

TI Synthesis of new substituted sulfonylhydrazinecarboxamides and  
 sulfonylhydrazinecarbothioamides having antifungal and antibacterial  
 activities

AU Nalavde, Yogesh Madhukar; Joshi, Vidya

CS C C Shroff Research Institute, Mumbai, 400 062, India

SO Indian Journal of Chemistry, Section B: Organic Chemistry Including  
 Medicinal Chemistry (2000), 39B(1), 76-79

CODEN: IJSBDB; ISSN: 0376-4699

PB National Institute of Science Communication, CSIR

DT Journal

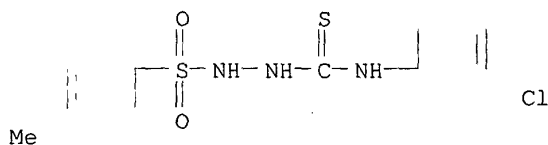
LA English

CC 25-13 (Benzene, Its Derivatives, and Condensed Benzenoid  
 Compounds)

Section cross-reference(s): 1, 10

AB P-Toluenesulfonylhydrazide on condensation with substituted Ph isocyanates  
 and substituted Ph isothiocyanates gives N,2-disubstituted  
 sulfonylhydrazinecarboxamides and N,2-disubstituted  
 sulfonylhydrazinecarbothioamides, resp. Both sets of products were

- bactericidal against *S.aureus* and *S.typhi*; one compd. shows fungicidal activity against *T.mentagrophytes* and *T.rubrum*.
- ST sulfonylhydrazinecarboxamide prepn bactericidal fungicidal activity;  
sulfonylhydrazinecarbothioamide prepn bactericidal fungicidal activity;  
bactericidal fungicidal activity sulfonylhydrazinecarboxamide  
sulfonylhydrazinecarbothioamide
- IT Antibacterial agents  
Fungicides  
(prepn. and bactericidal and fungicidal activity of  
sulfonylhydrazinecarboxamides and sulfonylhydrazinecarbothioamides)
- IT 66884-31-9P 66884-32-0P 92432-45-6P  
131574-10-2P 158532-38-8P 158532-39-9P  
203718-69-8P 203718-74-5P 281211-73-2P  
284488-49-9P 286378-09-4P 286378-10-7P  
286378-11-8P 286378-12-9P 286378-13-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and bactericidal and fungicidal activity of  
sulfonylhydrazinecarboxamides and sulfonylhydrazinecarbothioamides)
- IT 95-51-2, 2-Chloroaniline 98-16-8, 3-Trifluoromethylaniline 106-47-8,  
4-Chloroaniline, reactions 108-42-9, 3-Chloroaniline 108-91-8,  
Cyclohexylamine, reactions 348-54-9, 2-Fluoroaniline 371-40-4,  
4-Fluoroaniline 372-19-0, 3-Fluoroaniline 608-27-5,  
2,3-Dichloroaniline 1576-35-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. and bactericidal and fungicidal activity of  
sulfonylhydrazinecarboxamides and sulfonylhydrazinecarbothioamides)
- IT 104-12-1P, 4-Chlorophenyl isocyanate 329-01-1P, 3-Trifluoromethylphenyl  
isocyanate 404-71-7P, 3-Fluorophenyl isocyanate 1195-45-5P,  
4-Fluorophenyl isocyanate 2131-55-7P, 4-Chlorophenyl isothiocyanate  
2909-38-8P, 3-Chlorophenyl isocyanate 3173-53-3P, Cyclohexyl isocyanate  
3320-83-0P, 2-Chlorophenyl isocyanate 16744-98-2P, 2-Fluorophenyl  
isocyanate 41195-90-8P, 2,3-Dichlorophenyl isocyanate  
97319-65-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and bactericidal and fungicidal activity of  
sulfonylhydrazinecarboxamides and sulfonylhydrazinecarbothioamides)
- RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
- (1) Damle, S; Chem Eng News 1993, V71, P4 HCAPLUS
  - (2) Friedman, L; Org Syntheses, Coll 1973, V5, P1055
  - (3) Furniss, B; Vogels Textbook of Practical Organic Chemistry 1978, P737
  - (4) Hasan, R; Pesticide Science 1994, V42, P293
  - (5) Kurihara, T; Tohoku Yakka Daigaku Kenkyu Nempo 1969, V53 HCAPLUS
  - (6) Lozanova, K; Dokl Bulg Akad Nauk 1991, V44, P115 HCAPLUS
  - (7) Rodger, S; GB 2276382 1994 HCAPLUS
  - (8) Schraufstatter, E; Acta Pathologica et Microbiologica, Scandinavica, Supplementum 1955, V104, P49
  - (9) Tomayo, M; Bull Soc Chim Fr 1964, V2, P248
  - (10) United States Rubber Co; Neth Appl 6, 515, 582 1966
  - (11) Wright, J; J Med Pharm Chem 1962, V5, P815 HCAPLUS
- IT 66884-31-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and bactericidal and fungicidal activity of  
sulfonylhydrazinecarboxamides and sulfonylhydrazinecarbothioamides)
- RN 66884-31-9 HCAPLUS
- CN Benzenesulfonic acid, 4-methyl-, 2-[[[(3-chlorophenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



L48 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1999:808174 HCAPLUS  
 DN 132:165990  
 TI Protocols for amide high-speed analoging. Preparation of novel, small molecule cathepsin D inhibitors  
 AU Chen, Jinshan; Dixon, Brian R.; Dumas, Jacques; Brittelli, David  
 CS Bayer Research Center, Department of Chemistry Research, Pharmaceutical Division, Bayer Corporation, West Haven, CT, 06516, USA  
 SO Tetrahedron Letters (1999), 40(52), 9195-9199  
 CODEN: TELEAY; ISSN: 0040-4039  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 CC 25-19 (**Benzene**, Its Derivatives, and Condensed **Benzenoid** Compounds)  
 Section cross-reference(s): 1, 7  
 OS CASREACT 132:165990  
 AB Procedures for soln.-phase parallel synthesis of new, small mol. cathepsin D inhibitors by the coupling of acyl chlorides, sulfonyl chlorides and carboxylic acids with N nucleophiles were established using polymer-bound reagents to facilitate the chem. and/or to efficiently scavenge the unreacted starting materials and reaction byproducts. Ag(I) benzoate was used to facilitate the coupling of acyl chlorides with less reactive anilines. 2,3,5-(HO)Cl<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CO(NH)2COCH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>-4-SCF<sub>3</sub> was identified as a sub-micromolar cathepsin D inhibitor (IC<sub>50</sub> = 320 nM).  
 ST amide cathepsin D inhibitor combinatorial synthesis; library amide cathepsin inhibitor prepn; solid phase synthesis amide library  
 IT Acid halides  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acid chlorides; solid-phase synthesis of amide library)  
 IT Sulfonyl halides  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (chlorides; solid-phase synthesis of amide library)  
 IT Combinatorial library  
 (solid-phase synthesis of amide library)  
 IT Amines, reactions  
 Carboxylic acids, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (solid-phase synthesis of amide library)  
 IT Hydrazides  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (solid-phase synthesis of amide library)  
 IT Amides, preparation  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (solid-phase synthesis of amide library)  
 IT 9025-26-7, Cathepsin D  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (cathepsin D inhibitory activity of hydrazide)  
 IT 258520-64-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological



study); PREP (Preparation)  
 (solid-phase synthesis and cathepsin D inhibitory activity)  
 IT 107276-61-9P 258520-18-2P 258520-19-3P 258520-20-6P  
**258520-21-7P** 258520-22-8P 258520-23-9P 258520-24-0P  
 258520-25-1P 258520-26-2P 258520-27-3P 258520-28-4P  
**258520-29-5P** 258520-30-8P 258520-31-9P 258520-32-0P  
 258520-33-1P 258520-34-2P 258520-35-3P 258520-36-4P 258520-37-5P  
 258520-38-6P 258520-39-7P 258520-40-0P 258520-41-1P 258520-42-2P  
 258520-43-3P 258520-44-4P 258520-45-5P 258520-46-6P 258520-47-7P  
 258520-48-8P 258520-49-9P 258520-50-2P 258520-51-3P 258520-52-4P  
 258520-53-5P 258520-54-6P 258520-56-8P 258520-57-9P 258520-58-0P  
 258520-59-1P 258520-60-4P 258520-61-5P 258520-62-6P 258520-63-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (solid-phase synthesis of amide library)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

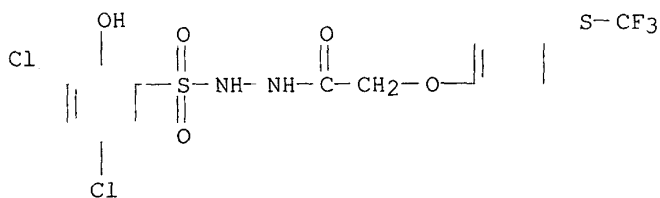
- (1) Booth, R; J Am Chem Soc 1997, V119, P4882 HCAPLUS
- (2) Desai, M; Tetrahedron Lett 1993, V34, P7685 HCAPLUS
- (3) Dumas, J; Bioorg Med Chem Lett 1999, V9, P2531 HCAPLUS
- (4) Dumas, J; Bioorg Med Chem Lett 1999, V9, P2531 HCAPLUS
- (5) Flynn, D; J Am Chem Soc 1997, V119, P4874 HCAPLUS
- (6) Gayo, L; Tetrahedron Lett 1996, V38, P513
- (7) Kaldor, S; Tetrahedron Lett 1996, V37, P7193 HCAPLUS
- (8) Kick, E; Chem Biol 1997, V4, P297 HCAPLUS
- (9) Lador, U; J Biol Chem 1994, V269, P18422 HCAPLUS
- (10) Lah, T; Breast Cancer Research and Treatment 1996, V39, P221 HCAPLUS
- (11) Lee, C; J Am Chem Soc 1998, V120, P9735 HCAPLUS
- (12) Parlow, J; Tetrahedron 1998, V54, P4013 HCAPLUS
- (13) Parlow, J; Tetrahedron Lett 1995, V36, P1395 HCAPLUS
- (14) Rochefort, H; Enzyme Protein 1996, V49, P106 HCAPLUS
- (15) Siegel, M; Tetrahedron Lett 1997, V38, P3357 HCAPLUS
- (16) Suto, M; Tetrahedron 1998, V54, P4141 HCAPLUS
- (17) Takimoto, S; Bull Chem Soc Jpn 1976, V49, P2335 HCAPLUS
- (18) Whitesitt, C; Bioorg Med Chem Lett 1996, V6, P2157 HCAPLUS

IT **258520-21-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (solid-phase synthesis of amide library)

RN 258520-21-7 HCAPLUS

CN Acetic acid, [4-[(trifluoromethyl)thio]phenoxy]-, 2-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]hydrazide (9CI) (CA INDEX NAME)



L48 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:525097 HCAPLUS

DN 131:299352

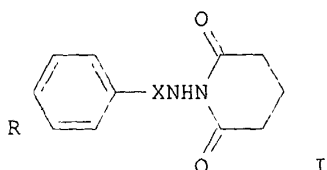
TI Synthesis and biological activity of acyl- and sulfonylhydrazides of glutaric acid and its imides and salts

AU Chernikh, V. P.; Shemchuk, L. A.; Gritsenko, I. S.; Ivanova, I. L.; Goryachii, V. D.; Tyukin, N. M.; Kovalenko, S. M.

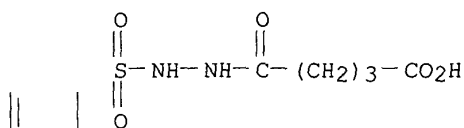
CS Ukr. Farm. Akad., Ukraine

SO Farmatsevtichnii Zhurnal (Kiev) (1998), (3), 46-50  
 CODEN: FRZKAP; ISSN: 0367-3057

PB Zdorov'ya  
 DT Journal  
 LA Ukrainian  
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1, 25  
 GI



- AB Title compds. such as  $RC_6H_4XNHNHCO(CH_2)_3CO_2R_1$  ( $R = 4-NO_2, 4-Br, 2-OH, 4-MeO, 4-Cl, 4-AcNH$ ;  $X = CO, SO_2$ ;  $R_1 = H, Na$ ) and I (same  $R, X$ ) were prepd. The compds. formed showed moderate diuretic, antiinflammatory, and analgesic activities.
- ST glutaric acid acylhydrazide sulfonylhydrazide prepn bioactivity; glutarimide benzamido benzenesulfonamido prepn bioactivity; diuretic glutaric hydrazide glutarimide deriv; antiinflammatory glutaric hydrazide glutarimide deriv; analgesic glutaric hydrazide glutarimide deriv
- IT Analgesics  
 Anti-inflammatory agents  
 Diuretics  
 (acyl- and sulfonylhydrazides of glutaric acid and its imides and salts)
- IT 161871-51-8P 161871-54-1P 161871-55-2P 162104-36-1P 162104-37-2P  
 182806-15-1P 182806-16-2P 182806-17-3P 182806-18-4P 182806-19-5P  
 247044-57-1P 247044-58-2P 247044-59-3P 247044-60-6P 247044-61-7P  
 247044-62-8P 247044-63-9P 247044-64-0P 247046-08-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepn. and bioactivity of)
- IT 209961-08-0P 247044-50-4P 247044-51-5P **247044-52-6P**  
**247044-53-7P** 247044-54-8P 247044-55-9P **247044-56-0P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn., cyclization, and bioactivity of)
- IT 108-55-4, Glutaric anhydride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction with benzoyl and benzenesulfonyl hydrazides)
- IT 80-17-1D, Benzenesulfonyl hydrazide, derivs. 613-94-5D, Benzoic acid hydrazide, derivs.  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction with glutaric anhydride)
- IT **247044-52-6P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn., cyclization, and bioactivity of)
- RN 247044-52-6 HCAPLUS
- CN Pentanedioic acid, mono[2-[(4-methoxyphenyl)sulfonyl]hydrazide] (9CI) (CA INDEX NAME)



MeO

L48 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:42740 HCAPLUS

DN 130:110060

TI Preparation of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release.

IN Broadhurst, Michael John; Johnson, William Henry; Walter, Daryl Simon

PA F. Hoffmann-La Roche A.-G., Switz.

SO Ger. Offen., 64 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM C07C311-49

ICS C07C259-06; C07C243-26; A61K031-195; A61K031-18; A61K031-505;  
C07D309-12; C07D227-02; C07D247-02; C07D333-06; C07D335-02;  
C07D277-62

ICA C07D521-00

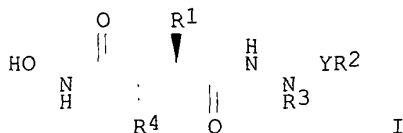
CC 25-22 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 27, 28

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19829229	A1	19990107	DE 1998-19829229	19980630
	US 6235787	B1	20010522	US 1998-98235	19980616
	WO 9901428	A1	19990114	WO 1998-EP3683	19980618
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9886273	A1	19990125	AU 1998-86273	19980618
	AU 725039	B2	20001005		
	EP 993442	A1	20000419	EP 1998-937498	19980618
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9810952	A	20000926	BR 1998-10952	19980618
	JP 2000513750	T2	20001017	JP 1999-506230	19980618
	ZA 9805469	A	19981230	ZA 1998-5469	19980623
	IT 1301792	B1	20000707	IT 1998-MI1441	19980624
	FR 2765219	A1	19981231	FR 1998-8124	19980626
	FR 2765219	B1	19991029		
	GB 2326881	A1	19990106	GB 1998-14027	19980629
	ES 2140348	A1	20000216	ES 1998-1359	19980629
	ES 2140348	B1	20001016		
	MX 9911668	A	20000531	MX 1999-11668	19991214
	NO 9906534	A	20000223	NO 1999-6534	19991229
PRAI	GB 1997-13833	A	19970630		
	GB 1998-3335	A	19980217		
	WO 1998-EP3683	W	19980618		

OS MARPAT 130:110060  
GI



- AB Title compds. [I; Y = CO, SO<sub>2</sub>; R<sub>1</sub> = alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl; R<sub>2</sub> = alkyl, haloalkyl, aralkyl, aralkenyl, aryl, alkoxy, alkoxycarbonyl, etc.; R<sub>3</sub> = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aralkyl, aralkenyl, aryl, heterocyclyl; R<sub>2</sub>R<sub>3</sub> = 5-7 membered cyclic amide, imide, sulfonamide, or urethane; R<sub>4</sub> = alkyl, alkenyl, cycloalkylalkyl, ArX, HetX, etc.; Ar = aryl; Het = heteroaryl; X = spacer], were prepd. Thus, (E)-2(R)-[1(S)-(hydroxycarbamoyl)-4-phenyl-3-butenyl]-2'-(methanesulfonyl)-4-methyl-2'-phenylvalerohydrazide (multistep prepn. given) inhibited TNF.alpha. and TGF.alpha. release with IC<sub>50</sub> = 437 nM and 210 nM, resp.
- ST hydroxycarbamoylalkylcarboxylic acid hydrazide prepn TNF TGF release inhibitor; tumor necrosis factor release inhibitor hydroxycarbamoylalkylcarboxylic acid hydrazide; transforming growth factor release inhibitor hydroxycarbamoylalkylcarboxylic acid hydrazide; antiinflammatory hydroxycarbamoylalkylcarboxylic acid hydrazide; antiarthritic hydroxycarbamoylalkylcarboxylic acid hydrazide
- IT Anti-inflammatory agents  
Antiarthritics  
Antipyretics  
(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)
- IT Hydrazides  
Hydroxamic acids  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)
- IT Tumor necrosis factors  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)
- IT Hemorrhage  
Multiple sclerosis  
Psoriasis  
Sepsis  
(treatment; prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)
- IT Transforming growth factors  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(.alpha.-; prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)
- IT 219612-20-1P 219612-22-3P 219612-25-6P 219612-27-8P 219612-31-4P  
219612-34-7P 219612-38-1P 219612-40-5P 219612-44-9P 219612-47-2P

219612-48-3P	219612-49-4P	219612-51-8P	219612-52-9P	219612-54-1P
219612-56-3P	219612-58-5P	219612-60-9P	219612-62-1P	219612-64-3P
219612-66-5P	219612-68-7P	219612-70-1P	219612-72-3P	219612-74-5P
219612-76-7P	219612-78-9P	219612-80-3P	219612-82-5P	219612-83-6P
219612-84-7P	219612-85-8P	219612-87-0P	219612-89-2P	219612-91-6P
219612-92-7P	219612-93-8P	219612-94-9P	219612-95-0P	219612-96-1P
219612-97-2P	219612-98-3P	219612-99-4P	219613-01-1P	219613-02-2P
219613-03-3P	219613-04-4P	219613-05-5P	219613-06-6P	219613-07-7P
219613-08-8P	219613-09-9P	219613-10-2P	219613-11-3P	219613-12-4P
219613-13-5P	219613-14-6P	219613-15-7P	219613-16-8P	219613-17-9P
219613-18-0P	219613-19-1P	219613-20-4P	219613-21-5P	219613-22-6P
219613-23-7P	219613-24-8P	219613-25-9P	219613-26-0P	219613-27-1P
219613-28-2P	219613-29-3P	219613-30-6P	219613-31-7P	219613-32-8P
219613-33-9P	219613-35-1P	219613-36-2P	219613-37-3P	219613-38-4P
219613-39-5P	219613-40-8P	219613-41-9P	219613-42-0P	219613-43-1P
219613-44-2P	219613-45-3P	219613-46-4P	219613-47-5P	219613-48-6P
219613-49-7P	219613-50-0P	219613-51-1P	219613-52-2P	219613-54-4P
219613-56-6P	219613-57-7P	219613-60-2P	219613-61-3P	219613-63-5P
<b>219613-64-6P</b>	219613-66-8P	219613-67-9P	219613-69-1P	
219613-71-5P	219613-74-8P	219613-76-0P	219613-80-6P	219613-83-9P
219613-86-2P	219613-87-3P	219613-88-4P	219613-89-5P	219613-90-8P
219613-91-9P	219613-92-0P	219613-93-1P	219613-94-2P	219613-95-3P
219613-96-4P	219613-97-5P	219613-98-6P	219613-99-7P	219614-00-3P
219614-01-4P	219614-02-5P	219614-03-6P	219614-04-7P	219614-05-8P
219614-06-9P	219614-07-0P	219614-08-1P	219614-09-2P	219614-10-5P
219614-11-6P	219614-12-7P	219614-13-8P	219614-15-0P	219614-16-1P
219614-18-3P	219614-20-7P			

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as inhibitors of tumor necrosis factor and transforming growth factor release)

IT 65-85-0, Benzoic acid, reactions 67-64-1, Acetone, reactions 78-84-2, Isobutyraldehyde 79-22-1, Methyl chloroformate 85-44-9, 1,3-Isobenzofurandione 90-11-9, 1-Bromonaphthalene 96-32-2, Methyl bromoacetate 97-72-3, Isobutyric anhydride 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-88-4, Benzoyl chloride 100-39-0, Benzyl bromide 100-63-0, Phenylhydrazine 103-71-9, Phenyl isocyanate, reactions 103-80-0, Phenylacetyl chloride 106-95-6, Allyl bromide, reactions 108-12-3, Isopentanoyl chloride 108-24-7 108-55-4, Glutaric anhydride 109-90-0, Ethyl isocyanate 110-02-1, Thiophene 120-92-3, Cyclopentanone 407-25-0, Trifluoroacetic anhydride 501-53-1, Benzyl chloroformate 502-42-1, Cycloheptanone 527-72-0, Thiophene-2-carboxylic acid 529-27-1, o-Tolylhydrazine 534-00-9, (S)-1-Bromo-2-methylbutane 540-51-2, 2-Bromoethanol 585-70-6, 5-Bromo-2-furoic acid 589-21-9, 4-Bromophenylhydrazine 622-33-3, O-Benzylhydroxylamine 630-19-3, Pivaldehyde 637-33-2, 3-Hydroxybenzylhydrazine 637-59-2, 1-Bromo-3-phenylpropane 870-46-2, tert-Butyl carbazate 890-98-2, Benzyl mandelate 932-86-5, 2-Bromoethylidenecyclohexane 939-26-4, 2-Bromomethylnaphthalene 1072-72-6, Tetrahydrothiopyran-4-one 1633-82-5, 3-Chloropropylsulfonyl chloride 1633-84-7, 4-Chloro-1-butan sulfonyl chloride 1939-99-7, Benzylsulfonyl chloride 2243-55-2, 1-Naphthylhydrazine 2386-60-9, 1-Butanesulfonyl chloride 2719-27-9, Cyclohexanecarbonyl chloride 3240-94-6, 4-(2-Chloroethyl)morpholine 4392-24-9, Cinnamyl bromide 4595-59-9 4801-27-8, 2-Bromoethyl chloroformate 4930-98-7, 2-Hydrazinopyridine 5781-53-3, Methyl oxalyl chloride 6482-24-2, 2-Bromoethyl methyl ether 6498-34-6, Cyclohexylhydrazine 6723-30-4 7051-34-5, Cyclopropylmethyl bromide 14190-59-1, 2-Thiazolecarboxylic acid 16629-19-9, Thiophene-2-sulfonyl chloride 21038-22-2, O-(4-Methoxybenzyl)hydroxylamine 21378-20-1 21691-53-2 29943-42-8, Tetrahydropyran-4-one 32064-67-8, tert-Butylhydrazine 37137-00-1,

2-Iodoethoxybenzene 40299-87-4, N-Bromoacetylmorpholine 41014-27-1,  
 2-Bromomethylbenzofuran 41879-39-4, O-tert-Butyldimethylsilylhydroxylami  
 ne 42504-87-0, Isobutylhydrazine 42726-73-8, tert-Butyl methyl  
 malonate 73870-24-3, 4-Bromomethylpyridine hydrobromide 75059-04-0,  
 4-Nitrocinnamyl bromide 79099-07-3, 1-tert-Butoxycarbonyl-4-piperidone  
 81701-30-6 87808-24-0 112245-04-2 112306-59-9 115754-94-4  
 134807-43-5 148415-75-2 157604-22-3 184948-24-1 191613-94-2  
 204637-77-4 219615-70-0 219615-71-1 219615-72-2 219615-73-3  
 219615-74-4 219615-75-5 219615-76-6 219615-77-7 219615-78-8  
 219615-79-9 219615-80-2 219615-81-3 219615-82-4 219615-83-5  
 219615-84-6 219615-85-7 219615-86-8 219615-88-0 219615-89-1  
 219615-90-4 219615-91-5 219615-92-6 219615-93-7 219615-95-9  
 219616-01-0 219616-02-1 219616-03-2 219616-04-3 219616-05-4  
 219616-06-5 219616-07-6 219616-08-7 219616-09-8 219616-10-1  
 219616-11-2 219616-12-3 219616-13-4 219616-14-5 219616-15-6  
 219616-16-7 219616-17-8 219616-18-9 219616-19-0 219616-20-3  
 219616-21-4 219616-22-5 219616-23-6 219616-24-7 219616-25-8  
 219616-26-9 219616-27-0 219616-29-2 219616-30-5 219616-31-6  
 219616-32-7 219616-33-8 219616-34-9 219616-35-0 219616-39-4  
 219616-40-7 219621-15-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as  
 inhibitors of tumor necrosis factor and transforming growth factor  
 release)

IT	145339-42-0P	148415-77-4P	184948-84-3P	219614-21-8P	219614-22-9P
	219614-23-0P	219614-24-1P	219614-25-2P	219614-26-3P	219614-27-4P
	219614-28-5P	219614-29-6P	219614-30-9P	219614-31-0P	219614-32-1P
	219614-33-2P	219614-34-3P	219614-35-4P	219614-36-5P	219614-37-6P
	219614-38-7P	219614-39-8P	219614-40-1P	219614-41-2P	219614-42-3P
	219614-43-4P	219614-44-5P	219614-45-6P	219614-46-7P	219614-47-8P
	219614-48-9P	219614-49-0P	219614-50-3P	219614-51-4P	219614-52-5P
	219614-53-6P	219614-54-7P	219614-55-8P	219614-56-9P	219614-57-0P
	219614-58-1P	219614-59-2P	219614-60-5P	219614-61-6P	219614-62-7P
	219614-63-8P	219614-64-9P	219614-65-0P	219614-66-1P	219614-67-2P
	219614-68-3P	219614-69-4P	219614-70-7P	219614-71-8P	219614-72-9P
	219614-73-0P	219614-74-1P	219614-75-2P	219614-76-3P	219614-77-4P
	219614-78-5P	219614-79-6P	219614-80-9P	219614-81-0P	219614-82-1P
	219614-84-3P	219614-85-4P	219614-86-5P	219614-87-6P	219614-88-7P
	219614-90-1P	219614-91-2P	219614-92-3P	219614-93-4P	219614-95-6P
	219614-97-8P	219614-98-9P	219614-99-0P	219615-00-6P	219615-01-7P
	219615-02-8P	219615-03-9P	219615-04-0P	219615-05-1P	219615-06-2P
	219615-07-3P	219615-08-4P	219615-09-5P	219615-10-8P	219615-11-9P
	219615-12-0P	219615-13-1P	219615-14-2P	219615-15-3P	219615-16-4P
	219615-17-5P	219615-18-6P	219615-19-7P	219615-20-0P	219615-21-1P
	219615-22-2P	219615-23-3P	219615-24-4P	219615-25-5P	
	<b>219615-26-6P</b>	<b>219615-27-7P</b>	219615-29-9P	219615-31-3P	
	219615-32-4P	219615-33-5P	219615-34-6P	219615-35-7P	219615-36-8P
	219615-37-9P	219615-38-0P	219615-39-1P	219615-40-4P	219615-41-5P
	219615-42-6P	219615-43-7P	219615-44-8P	219615-45-9P	219615-46-0P
	219615-47-1P	219615-48-2P	219615-49-3P	219615-50-6P	219615-51-7P
	219615-52-8P	219615-53-9P	219615-54-0P	219615-55-1P	219615-56-2P
	219615-57-3P	219615-58-4P	219615-59-5P	219615-60-8P	219615-61-9P
	219615-62-0P	219615-63-1P	219615-64-2P	219615-65-3P	219615-66-4P
	219615-67-5P	219615-68-6P	219615-69-7P	219615-87-9P	219615-94-8P
	219615-98-2P	219616-28-1P	219616-36-1P	219616-37-2P	219616-38-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as  
 inhibitors of tumor necrosis factor and transforming growth factor  
 release)

IT **219613-64-6P**

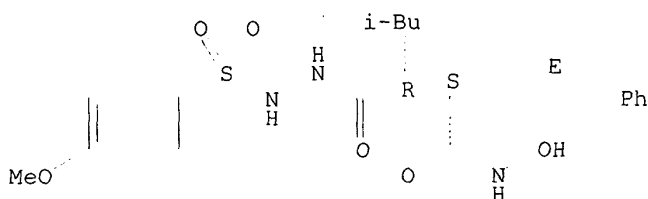
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of hydroxycarbamoylalkylcarboxylic acid hydrazides as  
inhibitors of tumor necrosis factor and transforming growth factor  
release)

RN 219613-64-6 HCAPLUS

CN 5-Hexenoic acid, 3-[(hydroxyamino)carbonyl]-2-(2-methylpropyl)-6-phenyl-,  
2-[(4-methoxyphenyl)sulfonyl]hydrazide, (2R,3S,5E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L48 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:144326 HCAPLUS

DN 128:192426

TI Synthesis and antineoplastic activity of 1-(4-toluensulfonyl)-4-arylsemicarbazides

AU Asis, Silvia E.; Bruno, Ana M.; Gaozza, Carlos H.

CS Centro Sintesis y Estudio de Nuevos Compuestos Antineoplasticos, Departamento de Quimica Organica, Facultad de Farmacia y Bioquimica, Universidad de Buenos Aires, Buenos Aires, 1113, Argent.

SO Acta Farmaceutica Bonaerense (1997), 16(4), 209-214

CODEN: AFBODJ; ISSN: 0326-2383

PB Colegio de Farmaceuticos de la Provincia de Buenos Aires

DT Journal

LA Spanish

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1

AB 4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNHCONHC<sub>6</sub>H<sub>4</sub>R [R = H, 4-Cl, 4-Me, 4-OMe, 3-CF<sub>3</sub>, 4-NO<sub>2</sub>; C<sub>6</sub>H<sub>4</sub>R = 1-naphthyl], structurally related to the Sulofenur family, were synthesized from RC<sub>6</sub>H<sub>4</sub>NCS and 4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNH<sub>2</sub>, followed by oxidn., or directly from RC<sub>6</sub>H<sub>4</sub>NCO, and evaluated as antineoplastic agents. 4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNHCONHC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-4 (I) was active against a variety of human tumors. DNA binding was assayed employing an improved UV method and all compds. exhibited no affinity to calf thymus DNA. Redox properties of I were also studied by cyclic voltammetry.

ST aryltosylsemicarbazide prepn antineoplastic; semicarbazide aryltosyl prepn antineoplastic

IT Antitumor agents

(prepn. and antineoplastic activity of aryl(toluensulfonyl)semicarbazides)

IT 28744-07-2P 131574-09-9P 131574-10-2P

203718-68-7P 203718-69-8P 203718-70-1P

203718-71-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and antineoplastic activity of aryl(toluensulfonyl)semicarbazides)

IT 86-84-0, 1-Naphthyl isocyanate 100-28-7, 4-Nitrophenyl isocyanate

103-72-0, Phenyl isothiocyanate 622-59-3, 4-Methylphenyl isothiocyanate

1576-35-8, Tosylhydrazine 1840-19-3, 3-Trifluoromethylphenyl

isothiocyanate 2131-55-7, 4-Chlorophenyl isothiocyanate 2284-20-0,  
4-Methoxyphenyl isothiocyanate  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. and antineoplastic activity of aryl(toluensulfonyl)semicarbazid  
es)

IT 28744-12-9P 66884-27-3P 66884-29-5P

66884-32-0P 203718-74-5P

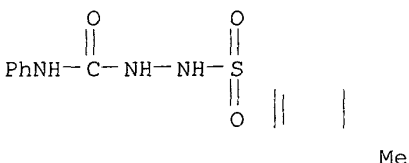
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and antineoplastic activity of aryl(toluensulfonyl)semicarbazid  
es)

IT 28744-07-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation)  
(prepn. and antineoplastic activity of aryl(toluensulfonyl)semicarbazid  
es)

RN 28744-07-2 HCAPLUS

CN Hydrazinecarboxamide, 2-[(4-methylphenyl)sulfonyl]-N-phenyl- (9CI) (CA  
INDEX NAME)



L48 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:684387 HCAPLUS

DN 127:331751

TI Preparation of peptidyl compounds having matrix metalloproteinase and  
tumor necrosis factor .alpha. inhibitory activity

IN Baxter, Andrew Douglas; Owen, David Alan; Montana, John Gary; Watson,  
Robert John; Keily, John Fraser

PA Chiroscience LLtd., UK; Baxter, Andrew Douglas; Owen, David Alan; Montana,  
John Gary; Watson, Robert John; Keily, John Fraser

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT **Patent**

LA English

IC ICM C07D209-48

ICS C07C323-60; C07C327-32; A61K031-18; A61K031-22; A61K031-40

CC 34-3 (Amino Acids, Peptides, and Proteins)

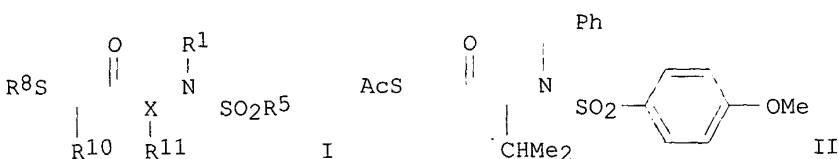
Section cross-reference(s): 1, 25, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9737973	A1	19971016	WO 1997-GB957	19970404
	W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2247964	AA	19971016	CA 1997-2247964	19970404
	AU 9723023	A1	19971029	AU 1997-23023	19970404

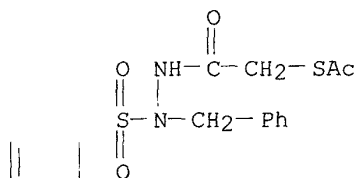


AU 718438 B2 20000413  
 EP 891328 A1 19990120 EP 1997-915605 19970404  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI  
 JP 2000508639 T2 20000711 JP 1997-535962 19970404  
 US 6114372 A 20000905 US 1998-155695 19981002  
 PRAI GB 1996-7119 A 19960404  
 WO 1997-GB957 W 19970404  
 OS MARPAT 127:331751  
 GI



- AB Peptidyl compds. I [X = CH, N; R1 = C1-6 alkyl, C2-6 alkenyl, aryl, C1-6 alkylaryl, heteroaryl, C1-6 alkylheteroaryl, C3-6 cycloalkyl, C1-6 alkyl-C3-6 cycloalkyl, C4-6 heterocycloalkyl, C1-6 alkyl-C4-6 heterocycloalkyl, C1-6 alkyl-COR2, C1-6 alkyl-AR3; A = O, NR3, S(O)n; n = 0-2; R3 = H, C1-4 alkyl, aryl, heteroaryl, C1-4 alkylaryl, C1-4 alkylheteroaryl; R2 = OR4, NR42; R4 = H, C1-4 alkyl; R5 = optionally R6-substituted aryl, heteroaryl, C1-4 alkylaryl, C1-4 alkylheteroaryl, C1-4 alkyl-C3-6 cycloalkyl, C4-6 heterocycloalkyl, C1-4 alkyl-C4-6 heterocycloalkyl; R6 = halo, C1-6 alkyl, aryl, heteroaryl, AR3, NR3R7, COR9, SO2NR32, COR4, CONR32, amidine, guanidine; R7 = substituted acyl, alkoxy carbonyl, sulfonyl, aminocarbonyl; R8 = H, COR9; R9 = C1-4 alkyl, aryl, heteroaryl, C1-4 alkylaryl, C1-4 alkylheteroaryl; R10, R11 = independently H, optionally substituted C1-6 alkyl, aryl, C1-6 alkylaryl, heteroaryl, C1-6 alkylheteroaryl, C3-6 cycloalkyl, C1-6 alkyl-C3-6 cycloalkyl, C4-6 heterocycloalkyl, C1-4 alkyl-C4-6 heterocycloalkyl], and salt, solvates, and hydrates thereof, having matrix metalloproteinase (MMP) and tumor necrosis factor .alpha. (TNF.alpha.) inhibitory activity are described. Thus, sequential reaction of N-benzyl-N-(4-methoxyphenylsulfonyl)-DL-valine (prepn. from DL-valine given) with CH2N2 and HBr gave bromomethyl ketone II, (R = Br), which underwent substitution with potassium thioacetate to give acetylmercapto deriv. II (R = SAc).
- ST matrix metalloproteinase inhibitor peptidyl thiol prepn; tumor necrosis factor peptidyl inhibitor prepn
- IT Tumor necrosis factors  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor necrosis factor .alpha. inhibitory activity)
- IT 197965-84-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor necrosis factor .alpha. inhibitory activity)
- IT 197965-83-6P 197965-85-8P 197965-86-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor necrosis factor .alpha. inhibitory activity)
- IT 141907-41-7, Matrix metalloproteinase 177529-10-1, L-Selectin sheddase  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL

(Biological study)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor  
 necrosis factor .alpha. inhibitory activity)  
 IT 98-68-0, 4-Methoxybenzenesulfonyl chloride 516-06-3, DL-Valine  
 10387-40-3, Potassium thioacetate 10553-78-3, Acetylthioacetyl chloride  
 20570-96-1, Benzylhydrazine dihydrochloride 179090-37-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor  
 necrosis factor .alpha. inhibitory activity)  
 IT 197965-87-0P **197965-88-1P** 197965-89-2P 197965-90-5P  
 197965-91-6P 197965-92-7P 197965-93-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT,  
 (Reactant or reagent)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor  
 necrosis factor .alpha. inhibitory activity)  
 IT **197965-84-7P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); RCT (Reactant); **THU (Therapeutic use);**  
**THU (Therapeutic use);** BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (prepn. of peptidyl compds. having matrix metalloproteinase and tumor  
 necrosis factor .alpha. inhibitory activity)  
 RN 197965-84-7 HCAPLUS  
 CN Acetic acid, (acetylthio)-, 2-[(4-methoxyphenyl)sulfonyl]-2-  
 (phenylmethyl)hydrazide (9CI) (CA INDEX NAME)



MeO

L48 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN **1997:421308** HCAPLUS  
 DN **127:34521**  
 TI Preparation of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl  
 protease inhibitors  
 IN Carr, Thomas Joseph; Desjarlais, Renee Louise; Gallagher, Timothy Francis;  
 Halbert, Stacie Marie; Oh, Hye-Ja; Thompson, Scott Kevin; Veber, Daniel  
 Frank; Yamashita, Dennis Shinji; et al.  
 PA USA  
 SO PCT Int. Appl., 253 pp.  
 CODEN: PIXXD2  
 DT **Patent**  
 LA English  
 IC ICM C07D277-56  
 ICS A61K031-425  
 CC 34-3 (Amino Acids, Peptides, and Proteins)  
 Section cross-reference(s): 1, 28  
 FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716433	A1	19970509	WO 1996-US18000	19961030
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG,				
KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG,				
SI, SK, TR, TT, UA, US, US, US, US, US, US, US, US, US, US,				
US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,  
 MR, NE, SN, TD, TG

ZA 9609078	A	19980429	ZA 1996-9078	19961029
AU 9711180	A1	19970522	AU 1997-11180	19961030
CN 1207095	A	19990203	CN 1996-199284	19961030
BR 9612344	A	19990713	BR 1996-12344	19961030
EP 934291	A1	19990811	EP 1996-941981	19961030

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, FI, RO

NO 9801938	A	19980629	NO 1998-1938	19980429
US 5998470	A	19991207	US 1999-290958	19990413
US 6057362	A	20000502	US 1999-330287	19990611
US 6232342	B1	20010515	US 1999-330451	19990611
US 6284777	B1	20010904	US 2000-552616	20000419
US 6331542	B1	20011218	US 2000-551968	20000419
NO 2000006716	A	19980629	NO 2000-6716	20001229
NO 2000006717	A	19980629	NO 2000-6717	20001229
NO 2000006718	A	19980629	NO 2000-6718	20001229
CN 1341590	A	20020327	CN 2001-104787	20010220
CN 1341592	A	20020327	CN 2001-104788	20010220
CN 1341593	A	20020327	CN 2001-104789	20010220
US 2002077455	A1	20020620	US 2001-839410	20010420
US 2002173469	A1	20021121	US 2002-160314	20020530

PRAI US 1995-8108P P 19951030  
 US 1995-7473P P 19951122  
 US 1995-8992P P 19951221  
 US 1996-13747P P 19960320  
 US 1996-13748P P 19960320  
 US 1996-13764P P 19960320  
 US 1996-17455P P 19960517  
 US 1996-17892P P 19960517  
 US 1996-22047P P 19960722  
 US 1996-23494P P 19960807  
 WO 1996-US18000 W 19961030  
 US 1997-793915 A3 19970214  
 US 1998-793915 B3 19980430  
 US 1999-330284 B1 19990611  
 US 1999-330305 B1 19990611  
 US 2000-633700 B1 20000807

OS MARPAT 127:34521

AB Title compds. of formula D-CO-Q [D = CbzNHCH(Bu-i), Cbz-Leu-NHCH(Bu-i),  
 4-PhOC6H4SO2NHCH2, Cbz-Leu-NHNH, etc.; Q = NHCH(Bu-i)(2-carboxythiazol-4-  
 yl), NHCH(Bu-i)(4-carboethoxythiazol-2-yl), NHNHCOCH(Bu-i)NHCBz,  
 CH2NHSO2C6H4-4-OPh, etc.; Cbz = PhCH2O2C] and pharmaceutical compns. of  
 such compds., which inhibit proteases, including cathepsin K (no data)  
 were prepd. Such compds. are particularly useful for treating diseases of  
 excessive bone loss or cartilage or matrix degrdn., e.g. osteoporosis,  
 periodontitis, and arthritis. For example, Cbz-Leu-Leu-CH2Br was treated  
 with H2NCSCo2Et in refluxing ethanol for 4 h to give Cbz-Leu-NHCH(Bu-i)(2-  
 carboethoxythiazol-4-yl), which was saponified by treatment with sodium  
 hydroxide in THF to yield title compd. Cbz-Leu-NHCH(Bu-i)(2-carboxythiazol-  
 4-yl).

ST peptidyl hydrazide prepn protease inhibitor; cathepsin K inhibitor peptide  
 analog prepn

IT Cartilage  
 Cartilage  
 (degeneration; prepn. of hydrazidyl, bis-hydrazidyl, and  
 bis-aminomethyl carbonyl protease inhibitors for treating)

IT Gingiva  
 (gingivitis; prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl  
 carbonyl protease inhibitors for treating)

IT Periodontium

(periodontitis; prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors for treating)

IT Peptides, preparation  
Peptidomimetics  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl)

IT Hydrazides  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

IT Bone, disease  
Osteoarthritis  
Osteoporosis  
Rheumatoid arthritis  
(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors for treating)

IT

3069-78-1P	190141-94-7P	190141-95-8P	190141-96-9P	190141-97-0P
190141-98-1P	190142-16-6P	190142-17-7P	190142-18-8P	190657-00-2P
190657-01-3P	190657-02-4P	190657-03-5P	190657-04-6P	190657-05-7P
190657-06-8P	190657-07-9P	190657-08-0P	190657-09-1P	190657-10-4P
190657-11-5P	190657-12-6P	190657-13-7P	190657-14-8P	190657-15-9P
190657-16-0P	190657-17-1P	190657-18-2P	190657-19-3P	190657-20-6P
190657-21-7P	190657-22-8P	190657-23-9P	190657-24-0P	190657-25-1P
190657-28-4P	190657-30-8P	190657-31-9P	190657-34-2P	190657-37-5P
190657-38-6P	190657-39-7P	190657-40-0P	190657-41-1P	190657-42-2P
190657-43-3P	190657-44-4P	190657-47-7P	190657-50-2P	190657-51-3P
190657-53-5P	190657-55-7P	190657-56-8P	190657-58-0P	190657-60-4P
190657-61-5P	190657-63-7P	190657-65-9P	190657-66-0P	190657-67-1P
190657-68-2P	190657-69-3P	190657-70-6P	190657-71-7P	190657-72-8P
<b>190657-73-9P</b>	190657-74-0P	190657-75-1P	190657-76-2P	
190657-77-3P	190657-78-4P	190657-79-5P	190657-80-8P	190657-81-9P
190657-82-0P	190657-83-1P	190657-84-2P	190657-85-3P	190657-86-4P
190657-87-5P	190657-88-6P	190657-89-7P	190657-90-0P	190657-91-1P
190657-92-2P	190657-93-3P	190657-94-4P	190657-95-5P	190657-96-6P
190657-97-7P	190657-98-8P	190657-99-9P	190658-00-5P	190658-01-6P
190658-02-7P	190658-03-8P	190658-04-9P	190658-05-0P	190658-06-1P
190658-07-2P	190658-08-3P	190658-09-4P	190658-10-7P	190658-11-8P
190658-12-9P	190658-13-0P	190658-14-1P	190658-15-2P	190658-16-3P
190658-17-4P	190658-18-5P	190658-19-6P	190658-20-9P	190658-21-0P
190658-22-1P	190658-23-2P	190658-24-3P	190658-25-4P	190658-26-5P
190658-27-6P	190658-28-7P	190658-29-8P	190658-30-1P	190658-31-2P
190658-32-3P	190658-33-4P	190658-34-5P	190658-35-6P	190658-36-7P
190658-37-8P	190658-38-9P	190658-39-0P	190658-40-3P	190658-41-4P
190658-42-5P	190658-43-6P	190658-44-7P	190658-45-8P	190658-46-9P
190658-47-0P	190658-48-1P	190658-49-2P	190658-50-5P	190658-51-6P
190658-52-7P	190658-54-9P	190658-56-1P	190658-58-3P	190658-59-4P
190658-61-8P	190658-63-0P	190658-66-3P	190658-67-4P	190658-70-9P
190658-73-2P	190658-76-5P	190658-79-8P	190658-84-5P	190658-87-8P
190658-90-3P	190658-91-4P	190658-94-7P	190658-98-1P	190658-99-2P
190659-00-8P	190659-01-9P	190659-02-0P	190659-03-1P	190659-04-2P
190659-05-3P	190659-06-4P	190659-07-5P	190659-08-6P	190659-09-7P
190659-10-0P	190659-11-1P	190659-12-2P	190659-13-3P	190659-14-4P
190659-15-5P	190659-16-6P	190659-17-7P	190659-18-8P	190659-19-9P
190659-20-2P	190659-21-3P	190659-22-4P	190659-23-5P	190659-26-8P
190659-27-9P	190659-28-0P	190659-29-1P	190659-30-4P	190659-31-5P
190659-32-6P	190659-33-7P	190659-34-8P	190659-35-9P	190659-36-0P
190659-37-1P	190659-38-2P	190659-39-3P	190659-40-6P	190659-41-7P
190659-42-8P	190659-43-9P	190659-44-0P	190659-45-1P	190659-46-2P
190659-47-3P	190659-48-4P	190659-49-5P	190659-50-8P	190659-51-9P

190659-52-0P 190659-53-1P 190659-54-2P 190659-55-3P 190659-56-4P  
 190659-57-5P 190659-58-6P 190659-60-0P 190659-61-1P 190659-62-2P  
 190659-64-4P 190659-66-6P 190659-67-7P 190659-69-9P 190659-71-3P  
 190659-73-5P 190659-75-7P 190659-77-9P 190659-78-0P 190659-79-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

IT 190659-80-4P 190659-82-6P 190659-84-8P 190659-86-0P 190659-88-2P  
 190659-90-6P 190659-92-8P 190659-94-0P 190659-95-1P 190659-97-3P  
 190659-99-5P 190660-01-6P 190660-03-8P 190660-05-0P 190660-08-3P  
 190660-10-7P 190660-12-9P 190660-14-1P 190660-16-3P 190660-18-5P  
 190660-20-9P 190660-22-1P 190660-24-3P 190660-26-5P 190660-28-7P  
 190660-30-1P 190660-32-3P 190660-34-5P 190660-36-7P 190660-38-9P  
 190660-40-3P 190660-42-5P 190660-44-7P 190660-46-9P 190660-48-1P  
 190660-50-5P 190660-52-7P 190660-54-9P 190660-56-1P 190660-58-3P  
 190660-60-7P 190660-62-9P 190660-63-0P 190660-64-1P 190660-65-2P  
 190660-66-3P 190660-67-4P 190660-68-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

IT 37353-41-6, Cysteine protease 94716-09-3, Cathepsin k  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

IT 55-22-1, Isonicotinic acid, reactions 64-04-0, 2-Phenylethylamine  
 70-23-5, Ethyl bromopyruvate 85-48-3, 8-Quinoline sulfonic acid  
 86-59-9, 8-Quinoline carboxylic acid 86-76-0, 2-Bromodibenzofuran  
 92-67-1, 4-Aminobiphenyl 92-92-2, 4-Phenylbenzoic acid 95-56-7,  
 2-Bromophenol 97-69-8, N-Acetyl-alanine 98-80-6, Phenylboronic acid  
 98-97-5, Pyrazinecarboxylic acid 98-98-6, Picolinic acid 99-76-3,  
 Methyl 4-hydroxybenzoate 100-09-4, 4-Methoxybenzoic acid 100-55-0,  
 3-Pyridyl carbinol 101-55-3, 4-Phenoxyphenyl bromide 104-98-3  
 107-11-9, Allylamine 110-91-8, Morpholine, reactions 110-96-3  
 123-90-0, Thiomorpholine 475-11-6, N-Methyl-proline 501-52-0,  
 Hydrocinnamic acid 501-53-1, Benzyl chloroformate 501-89-3,  
 4-Carboxymethyl benzoic acid 532-55-8, Benzoyl isothiocyanate  
 541-53-7, Dithiobiuret 556-52-5, Glycidol 578-57-4, 2-Bromoanisole  
 586-95-8, 4-Pyridylcarbinol 586-98-1, 2-Pyridylcarbinol 616-29-5,  
 1,3-Diamino-propan-2-ol 625-43-4, N-Methylisobutylamine 627-37-2,  
 N-Methyl-N-allylamine 645-65-8, 4-Imidazolylacetic acid 646-07-1,  
 4-Methylpentanoic acid 1066-45-1, Trimethyltin chloride 1115-59-9  
 1118-68-9, N,N-Dimethylglycine 1123-00-8, Cyclopentylacetic acid  
 1129-28-8, Methyl 3-(bromomethyl)benzoate 1138-80-3 1142-20-7  
 1148-11-4 1161-13-3 1188-21-2, N-Acetyl-leucine 1586-00-1,  
 2-Benzylbenzyl alcohol 1592-38-7, 2-Naphthalenemethanol 1621-91-6,  
 1H-Pyrazole-3-carboxylic acid 1878-67-7, 3-Bromophenylacetic acid  
 2018-66-8, N-Benzoyloxycarbonyl-leucine 2113-57-7 2113-68-0, 4-Biphenyl  
 sulfonic acid 2150-44-9, Methyl 3,5-dihydroxybenzoate 2215-77-2,  
 4-Phenoxybenzoic acid 2417-72-3, Methyl 4-(bromomethyl)benzoate  
 2637-34-5, 2-Mercaptopyridine 2817-13-2 2928-43-0, 2-Biphenylmethanol  
 2991-28-8, 2,5-Difluorobenzoic acid 3017-69-4, Isobutenyl bromide  
 3060-46-6, N-Methyl-leucine 3179-63-3 3731-53-1, 4-Pyridylmethylamine  
 3886-08-6 4530-20-5 4688-76-0, 2-Biphenylboronic acid 4755-77-5,  
 Ethyl oxalyl chloride 5292-21-7, Cyclohexylacetic acid 5455-98-1,  
 N-(2,3-Epoxypropyl)phthalimide 5555-13-5 5651-55-8,  
 3-Benzoyloxy-4,5-dimethoxybenzoic acid 5728-52-9, 4-Biphenylacetic acid  
 7764-95-6 7801-71-0 10349-57-2, 6-Quinoline carboxylic acid  
 13826-35-2, 3-Phenoxybenzyl alcohol 13922-41-3, 1-Naphthyl boronic acid

14389-86-7, 2-Benzyloxybenzoic acid 15159-40-7, 4-Morpholinecarbonyl  
chloride 15761-38-3 16567-18-3, 8-Bromoquinoline 16982-21-1, Ethyl  
thiooxamate 18704-37-5, 8-Quinolinesulfonyl chloride 19438-10-9,  
Methyl 3-hydroxybenzoate 21691-44-1, N-Benzyloxycarbonyl-norvaline  
23095-31-0, 3,4-Dimethoxy-phenyl-sulfonyl chloride 23602-98-4,  
2-Dibenzofuransulfonyl chloride 26389-60-6, N-  
Cyclopropylmethylpropylamine 28862-79-5, N-Benzyloxycarbonyl-D-leucine  
32316-92-0, 2-Naphthylboronic acid 33099-08-0 35661-60-0 39608-30-5  
42918-86-5 53363-89-6 56946-83-9, 2,5-Dichlorothiophene-3-sulfonyl  
chloride 65489-71-6 68947-43-3, N-Methyl-piperidine-4-carboxylic acid  
83863-63-2, 2-Dibenzofuran-sulfonic acid 88398-93-0 127862-86-6  
161994-06-5, Propanedithiol 166964-37-0 175136-72-8 190661-76-8  
190661-77-9 190661-78-0 190661-79-1 190661-80-4 190661-81-5  
190661-82-6 190661-83-7 190661-85-9 190901-07-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl  
protease inhibitors)

IT 1623-92-3P 1623-93-4P, [1,1'-Biphenyl]-4-sulfonyl chloride 3504-37-8P  
4801-79-0P 7320-78-7P 13990-98-2P 17113-77-8P, 2-  
Trimethylstannylanisole 18153-53-2P 19520-74-2P 20777-79-1P  
21347-31-9P 23948-77-8P, [1,1'-Biphenyl]-3-acetic acid 27383-13-7P  
31575-75-4P 35026-08-5P 39570-63-3P 42384-22-5P 50637-26-8P  
50637-27-9P 51021-87-5P 53085-26-0P, Ethyl oxalamidrazonate  
63096-02-6P 65685-01-0P, [1,1'-Biphenyl]-3-sulfonyl chloride  
66715-65-9P, 2-Pyridinesulfonyl chloride 67451-81-4P 68314-54-5P  
69026-14-8P 70533-96-9P 73018-98-1P 75852-28-7P 77284-59-4P  
79678-37-8P 89376-18-1P 96929-05-4P 99701-60-7P 100367-77-9P  
101190-77-6P 111946-78-2P 111946-80-6P 115299-16-6P 115311-36-9P  
118252-75-8P 118252-77-0P 127942-30-7P 140157-44-4P 144255-33-4P  
150529-73-0P 154739-53-4P 168431-73-0P 171861-74-8P 172092-34-1P  
186693-25-4P 189811-19-6P 190142-08-6P 190142-09-7P 190142-10-0P  
190142-11-1P 190142-12-2P 190142-13-3P 190142-14-4P 190142-15-5P  
190660-69-6P 190660-70-9P 190660-72-1P 190660-73-2P 190660-74-3P  
190660-75-4P 190660-76-5P 190660-77-6P 190660-78-7P 190660-79-8P  
190660-81-2P 190660-82-3P 190660-83-4P 190660-84-5P 190660-85-6P  
190660-86-7DP, resin-bound 190660-87-8DP, resin-bound 190660-88-9P  
190660-89-0P 190660-90-3P 190660-91-4P 190660-92-5P 190660-93-6P  
190660-94-7P 190660-95-8P 190660-97-0P 190660-99-2P 190661-01-9P  
190661-03-1P 190661-08-6P 190661-10-0P 190661-13-3P 190661-15-5P  
190661-17-7P 190661-19-9P 190661-20-2P 190661-22-4P 190661-24-6P  
190661-25-7P 190661-26-8P 190661-27-9P 190661-28-0P 190661-29-1P  
190661-30-4P 190661-31-5P 190661-32-6P 190661-33-7P 190661-34-8P  
190661-35-9P 190661-36-0P 190661-37-1P 190661-38-2P 190661-39-3P  
190661-40-6P 190661-41-7P 190661-42-8P 190661-43-9P 190661-44-0P  
190661-45-1P 190661-46-2P 190661-47-3P 190661-48-4P 190661-49-5P  
190661-50-8P 190661-51-9P 190661-52-0P 190661-53-1P 190661-54-2P  
190661-55-3P 190661-56-4P 190661-57-5P 190661-58-6P 190661-60-0P  
190661-61-1P 190661-62-2P 190661-63-3P 190661-64-4P 190661-65-5P  
190661-66-6P 190661-67-7P 190661-68-8P 190661-69-9P 190661-70-2P  
190661-71-3P 190661-72-4P 190661-73-5P 190661-74-6P 190661-75-7P  
190900-97-1DP, resin-bound 190900-99-3DP, resin-bound 190901-05-4DP,  
resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl  
protease inhibitors)

IT 190657-73-9P

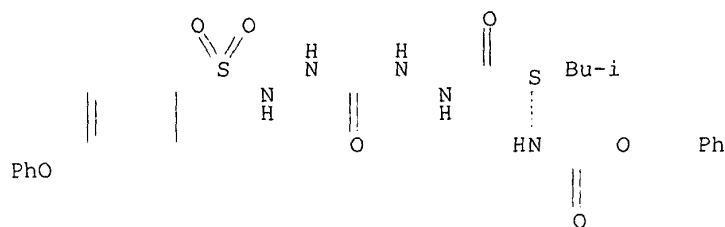
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl  
protease inhibitors)

RN 190657-73-9 HCAPLUS

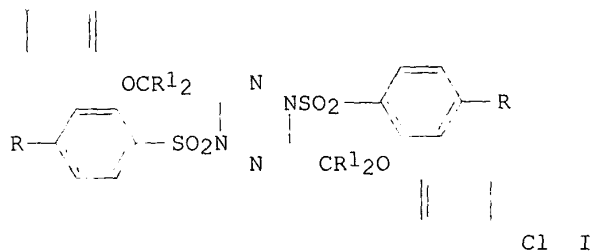
CN L-Leucine, N-[(phenylmethoxy)carbonyl]-, 2-[[2-[(4-phenoxyphenyl)sulfonyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



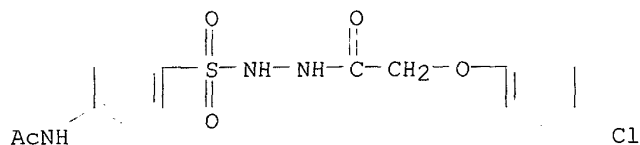
L48 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1989:212780 HCAPLUS  
 DN 110:212780  
 TI Synthesis and biological activity of 1-(p-chlorophenoxyalkanoyl)-2-arylsulfonylhydrazines and 3,6-di(p-chlorophenoxyalkyl)-1,4-diarylsulfonyl-1,4-dihydro-1,2,4,5-tetrazines  
 AU Nageswar, Y. V. D.; Murty, M. S. R.; Rao, A. Bhaskara; Ramalingam, T.; Sattur, P. B.  
 CS Reg. Res. Lab., Hyderabad, 500 007, India  
 SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1988), 27B(11), 1057-9  
 CODEN: IJSBDB; ISSN: 0376-4699  
 DT Journal  
 LA English  
 CC 28-20 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 25  
 OS CASREACT 110:212780  
 GI

Cl



AB A no. of title hydrazines 4-RC6H4SO2NHNHCOCR12OC6H4Cl-4 (R = H, Me, Cl, NHAc, R1 = H, Me) and a few title tetrazines I (R = H, Me, R1 = H, Me) were prepd. and screened for their biol. activities. Some of the compds. exhibit mild to moderate hypoglycemic and antiinflammatory activities.  
 ST chlorophenoxyalkanoylarylsulfonylhydrazine prepn hypoglycemic antiinflammatory; tetrazine bischlorophenoxyalkyl diarylsulfonyl hypoglycemic antiinflammatory  
 IT Antidiabetics and Hypoglycemics  
 Inflammation inhibitors  
 ((chlorophenoxyalkanoyl)arylsulfonylhydrazines and bis(chlorophenoxyalkanoyl)diarylsulfonyldihydro-tetrazines as)  
 IT 98-09-9, Phenylsulfonyl chloride 98-59-9 98-60-2 121-60-8

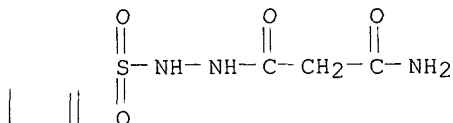
RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reactions of, with chlorophenoxyalkanoic acid hydrazides)  
 IT 2381-75-1, p-Chlorophenoxyacetic acid hydrazide 29771-66-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reactions of, with phenylsulfonyl chlorides)  
 IT 120513-12-4P 120513-13-5P 120513-14-6P 120513-15-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. and cyclodimerization of, with base)  
 IT 37049-73-3P 120513-09-9P 120513-10-2P 120513-11-3P  
 120513-16-8P 120513-17-9P 120513-18-0P 120513-19-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and hypoglycemic and antiinflammatory activities of)  
 IT 34088-34-1P 120513-06-6P 120513-07-7P 120513-08-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn., chlorodehydration, and hypoglycemic and antiinflammatory  
 activities of)  
 IT 37049-73-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and hypoglycemic and antiinflammatory activities of)  
 RN 37049-73-3 HCAPLUS  
 CN Acetic acid, (4-chlorophenoxy)-, 2-[[4-(acetylamino)phenyl]sulfonyl]hydraz  
 ide (9CI) (CA INDEX NAME)



L48 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1988:473104 HCAPLUS  
 DN 109:73104  
 TI Synthesis and biological activity of malonic acid arylsulfonylhydrazides  
 AU Chernykh, V. P.; Gritsenko, I. S.; Knyaz, E. M.; Berezhnyakova, A. I.;  
 Samura, B. A.  
 CS Khar'k. Gos. Farm. Inst., Kharkov, USSR  
 SO Farmatsevtichnii Zhurnal (Kiev) (1987), (6), 57-8  
 CODEN: FRZKAP; ISSN: 0367-3057  
 DT Journal  
 LA Ukrainian  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid  
 Compounds)  
 Section cross-reference(s): 1  
 AB Acylating p-RC6H4SO2NHNH2 (R = MeO, H, O2N, Br, HO2C, H2NSO2) with  
 ClCOCH2CO2Et in dioxane contg. pyridine gave 80-93% p-RC6H4SO2NHNHCOCH2COX  
 (I; same R, X = OEt), which were amidated with aq.-alc. NH3 to give 62-78%  
 I (same R, X = NH2) and sapon. to give 60-78% I (R = MeO, HO2C, H2NSO2; X  
 = OH). I had neurotropic, diuretic and antiinflammatory activity (no  
 data).  
 ST acylation sulfonylhydrazide malonyl chloride; arylsulfonyl malonhydrazide  
 prepn pharmacol; neurotropic arylsulfonyl malonhydrazide; diuretic  
 arylsulfonyl malonhydrazide; antiinflammatory arylsulfonyl malonhydrazide  
 IT Diuretics  
 Inflammation inhibitors  
 Psychotropics  
 ((arylsulfonyl)malonhydrazides)  
 IT 36239-09-5, Ethyl malonyl chloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)

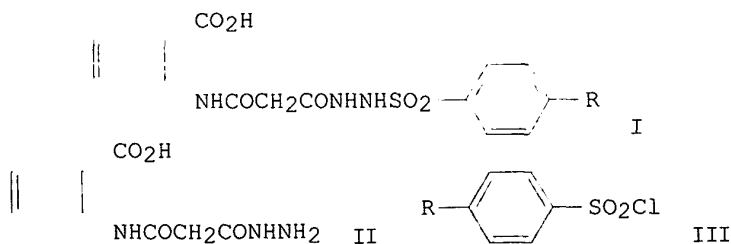


(acylation by, of arenesulfonhydrazides)  
 IT 80-17-1 1950-68-1 2297-64-5 2937-05-5 6391-97-5 114642-58-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of, with Et malonyl chloride)  
 IT 115542-32-0P 115542-33-1P 115542-34-2P 115542-35-3P  
 115542-36-4P 115542-37-5P 115542-38-6P  
 115542-39-7P 115542-40-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and pharmacol. of)  
 IT 16501-66-9P 115542-27-3P 115542-28-4P 115542-29-5P  
 115542-30-8P 115542-31-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn., pharmacol., sapon. and amidation of)  
 IT 115542-32-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and pharmacol. of)  
 RN 115542-32-0 HCAPLUS  
 CN Propanoic acid, 3-amino-3-oxo-, 2-[(4-methoxyphenyl)sulfonyl]hydrazide  
 (9CI) (CA INDEX NAME)



MeO

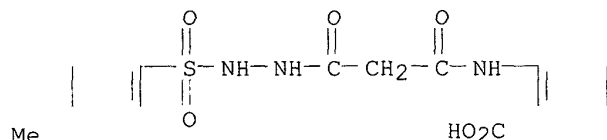
L48 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1988:431916 HCAPLUS  
 DN 109:31916  
 TI Search for neuroleptic agents among derivatives of .beta.-N-arenesulfohydrazides of malonic acid 2-carboxyphenylamide  
 AU Bezuglyi, P. O.; Treskach, V. I.; Ukrainets, I. V.; Samura, B. A.; Shaporenko, S. V.  
 CS Kharkov Pharm. Inst., Kharkov, USSR  
 SO Farmatsevtichnii Zhurnal (Kiev) (1988), (2), 37-40  
 CODEN: FRZKAP; ISSN: 0367-3057  
 DT Journal  
 LA Ukrainian  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 25  
 GI



AB Three title compds. (I; R = H, Me, or NHCO<sub>2</sub>Me) were prepd. by condensation

of II with III (R = H, Me, or NHCO<sub>2</sub>Me). This was done most effectively in a medium contg. NaOH to absorb evolved HCl. I were of low-to-moderate toxicity in mice. The greatest neuroleptic activity in cats (exceeding that of aminazine) was obsd. with I (R = H). Data on the diuretic activity of I are also presented.

- ST sulfohydrazide malonate deriv neuroleptic toxicity  
 IT Tranquilizers and Neuroleptics  
     (carboxyphenylamidomalonic acid arensulfohydrazides as)  
 IT Toxicity  
     (of carboxyphenylamidomalonic acid arensulfohydrazides)  
 IT 75205-50-4  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
         (condensation of, with aryl sulfonyl chlorides)  
 IT 98-09-9, Benzenesulfonyl chloride 98-59-9 21926-53-4  
     RL: BIOL (Biological study)  
         (condensation of, with carboxyphenylamidomalonic acid hydrazide)  
 IT 115150-36-2P 115150-37-3P 115150-38-4P  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
         (prepn. and neuroleptic activity of)  
 IT 115150-37-3P  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
         (prepn. and neuroleptic activity of)  
 RN 115150-37-3 HCAPLUS  
 CN Benzoic acid, 2-[[3-[2-[(4-methylphenyl)sulfonyl]hydrazino]-1,3-dioxopropyl]amino]- (9CI) (CA INDEX NAME)



- L48 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1988:221377 HCAPLUS  
 DN 108:221377  
 TI Synthesis and biological activity of arylsulfohydrazides of maleic and fumaric acids and methyl esters of arylsulfohydrazides of fumaric acid  
 AU Chernykh, V. P.; Gritsenko, I. S.; Stavnichuk, S. V.; Bereznyakova, A. I.; Popov, S. B.  
 CS Kharkov Pharm. Inst., Kharkov, USSR  
 SO Farmatsevtichnii Zhurnal (Kiev) (1987), (4), 42-5  
     CODEN: FRZKAP; ISSN: 0367-3057  
 DT Journal  
 LA Ukrainian  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
     Section cross-reference(s): 1  
 AB Treating p-RC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNH<sub>2</sub> (I; R = H, Br, O<sub>2</sub>N, MeO, HO<sub>2</sub>C) with maleic anhydride in AcOH gave 71-92% cis-p-RC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNHCOCH:CHCO<sub>2</sub>H (cis-II; same R), which could not be esterified with abs. MeOH contg. H<sub>2</sub>SO<sub>4</sub>. I (R = Br, O<sub>2</sub>N, MeO, HO<sub>2</sub>C, H<sub>2</sub>NSO<sub>2</sub>) reacted with trans-MeO<sub>2</sub>CCH:CHCOCl in dioxane contg. Et<sub>3</sub>N to give 46-74% trans-p-RC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNHCOCH:CHCO<sub>2</sub>Me (III; same R), which were sapond. with 5% aq. NaOH to give 79-86% trans-II (R = O<sub>2</sub>N, MeO, HO<sub>2</sub>C, H<sub>2</sub>NSO<sub>2</sub>). trans-II (R = H, Me) were prepd. analogously in 86-87% yield from III (same R). The IR spectra and LD<sub>50</sub> of II and III were

given. cis-II (R = H, MeO), trans-II (R = MeO, HO<sub>2</sub>C, H<sub>2</sub>NSO<sub>2</sub>) and III (R = MeO) were the only products with antiinflammatory activity, but most II had significant analgesic and anticoagulant activity.

ST sulfohydrazide maleic fumaric prepn pharmacol; hydrazide acyl sulfonyl prepn pharmacol; antiinflammatory acyl sulfonyl hydrazide; analgesic acyl sulfonyl hydrazide; anticoagulant acyl sulfonyl hydrazide

IT Analgesics  
Anticoagulants and Antithrombotics  
Inflammation inhibitors  
(maleic and fumaric sulfohydrazides)

IT Hydrazides  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(acyl sulfonyl, prepn., toxicity and pharmacol. of)

IT 108-31-6, reactions 17081-97-9, Methyl fumaroyl chloride  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation by, of arylsulfonyl hydrazides)

IT 1576-35-8, p-Tosyl hydrazide 114642-58-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation of, with Me fumaroyl chloride)

IT 80-17-1, Phenylsulfonyl hydrazide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation of, with maleic anhydride)

IT 1950-68-1, p-Methoxyphenylsulfonyl hydrazide 2297-64-5,  
p-Bromophenylsulfonyl hydrazide 2937-05-5, p-Nitrophenylsulfonyl  
hydrazide 6391-97-5, p-Carboxyphenylsulfonyl hydrazide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation of, with maleic anhydride and with Me fumaroyl chloride)

IT 100079-79-6P 114642-63-6P 114642-68-1P 114642-69-2P  
114642-70-5P 114642-71-6P 114642-72-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., toxicity and pharmacol. of)

IT 114642-64-7P 114642-65-8P 114642-66-9P  
114642-67-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., toxicity, pharmacol. and sapon. of)

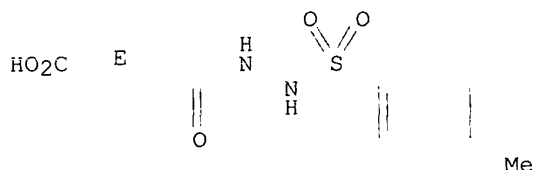
IT 94216-78-1P 114642-59-0P 114642-60-3P 114642-61-4P  
114642-62-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., toxicity, pharmacol., and attempted esterification of, with  
methanol)

IT 114642-68-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., toxicity and pharmacol. of)

RN 114642-68-1 HCAPLUS

CN 2-Butenedioic acid (2E)-, mono[2-[(4-methylphenyl)sulfonyl]hydrazide]  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



L48 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
AN 1985:5820 HCAPLUS  
DN 102:5820  
TI Synthesis and cholagogic activity of substituted amides, arenesulfamides,

acyl- and arenesulfohydrazides, of 4-hydroxyoxanylic acid

AU Petyunin, G. P.; Tarusin, A. D.; Drogozov, S. M.; Filippova, L. I.

CS Ukr. Inst. Usoversh. Vrachei, Kharkov, USSR

SO Khimiko-Farmatsevticheskii Zhurnal (1984), 18(6), 683-6

CODEN: KHFZAN; ISSN: 0023-1134

DT Journal

LA Russian

CC 25-13 (**Benzene**, Its Derivatives, and Condensed **Benzenoid** Compounds)

Section cross-reference(s): 1

OS CASREACT 102:5820

AB p-HOC6H4NHCOCOX (I; X = OEt) reacted with RNH2[R = H, decyl, allyl, PhCH2, o- and p-HOC6H4, 3,4-HO(HO2C)C6H3, PhSO2, p-MeOC6H4SO2, p-H2NC6H4SO2] to give 53-84% I (X = NHR; same R). I (X = NHNH2) reacted with R1Cl (R1 = Ac, Bz, p-MeC6H4CO, PhSO2, p-tosyl, p-AcOC6H4SO2) to give 57-71% I (X = NHNHR1; same R1). The IR and UV spectra and pKa values of I (X = NHR, NHNAR1) were interpreted. All I except I (X = NHCH2CH:CH2, NHSO2C6H4OMe-p) increased bile secretion in white rats, with I [X = NHC6H3(CO2H)OH-4,3](II) having the most activity. I (X = NHSO2C6H2NH2-p) increased cholesterol prodn., while I (X = NHC10H21), II and p-HOC6H4NHCO(CH2)4CONHC6H4-p decreased.

ST choleric amide sulfonamide hydrazide hydroxyoxanilic; oxanilamide hydroxy amide deriv

IT Choleric

RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydroxyoxanilic amides, arenesulfamides, and acyl- and arenesulfonylhydrazides)

IT Amidation  
(of hydroxyoxyanilate, in prepn. of choleric)

IT 111-50-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation by, of aminophenol, dianilide by)

IT 75-36-5 98-09-9 98-59-9 98-88-4 874-60-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation by, of hydroxyoxanilic hydrazide)

IT 40821-49-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(amidation of, in synthesis of choleric)

IT 63-74-1 65-49-6 95-55-6 98-10-2 100-46-9, reactions 107-11-9  
123-30-8 1129-26-6 2016-57-1 7664-41-7, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(amidation with, of Et hydroxyoxanilate)

IT 10187-22-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and choleric activity of)

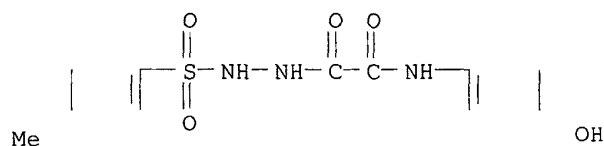
IT 79119-26-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

IT 19532-75-3P 21132-79-6P 93628-82-1P 93628-83-2P 93628-84-3P  
93628-85-4P 93628-86-5P 93628-87-6P 93628-88-7P 93628-89-8P  
93628-90-1P 93628-91-2P 93628-92-3P 93628-93-4P **93628-94-5P**  
**93628-95-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., spectra and choleric activity of)

IT **93628-94-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., spectra and choleric activity of)

RN 93628-94-5 HCAPLUS

CN Acetic acid, [(4-hydroxyphenyl)amino]oxo-, 2-[(4-methylphenyl)sulfonyl]hydrazide (9CI) (CA INDEX NAME)

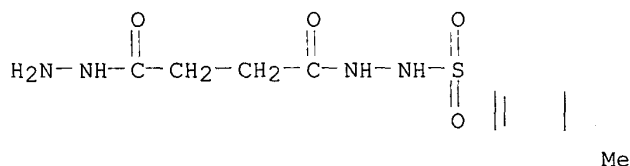


L48 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1984:490530 HCAPLUS  
 DN 101:90530  
 TI Synthesis and biological activity of aryl- and heterylhydrazones of succinate arenesulfohydrazides  
 AU Chernykh, V. P.; Gritsenko, I. S.; Zakharova, T. I.; Chubenko, V. O.; Kholupyak, I. Yu.  
 CS Khark. Derzh. Farm. Inst., Kharkov, USSR  
 SO Farmatsevtichnii Zhurnal (Kiev) (1984), (2), 64-5  
 CODEN: FRZKAP; ISSN: 0367-3057  
 DT Journal  
 LA Ukrainian  
 CC 25-19 (**Benzene**, Its Derivatives, and Condensed **Benzenoid** Compounds)  
 Section cross-reference(s): 1  
 AB p-RC6H4SO2NHNHCOCH2CH2CONHNZ (I; R = H, Me, MeO, Br, O2N; Z = H2) condensed with R1COR2 (R1 = Ph, 4-MeOC6H4, 2-HOC6H4, 2-furyl, 5-nitro-2-furyl, R2 = H; R1R2C: = isatin-3-ylidene) in refluxing EtOH to give 13 I (Z = :CR1R2; same R-R2) (II) in 80-95% yield. II had moderate diuretic, hypoglycemic, bactericidal and/or fungicidal activity.  
 ST condensation aldehyde ketone succinic hydrazide; hydrazone arylsulfonylsuccinic prepn pharmacol; diuretic arylsulfonylsuccinic hydrazone; hypoglycemic arylsulfonylsuccinic hydrazone; bactericide arylsulfonylsuccinic hydrazone; fungicide arylsulfonylsuccinic hydrazone  
 IT Antidiabetics and Hypoglycemics  
 Bactericides, Disinfectants, and Antiseptics  
 Diuretics  
 Fungicides and Fungistats  
 ((arylsulfonyl)succinic hydrazones)  
 IT Aldehydes, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reaction of, with (arylsulfonyl)succinic hydrazides)  
 IT Condensation reaction  
 (of (arylsulfonyl)succinic hydrazides with aldehydes and ketones)  
 IT 90-02-8, reactions 91-56-5 98-01-1, reactions 100-52-7, reactions 123-11-5, reactions 698-63-5, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reaction of, with (arylsulfonyl)succinic hydrazides)  
 IT 87362-08-1 87362-09-2 87362-12-7 87362-13-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reaction of, with aldehydes)  
 IT 87362-10-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation reaction of, with aldehydes and isatin)  
 IT 87362-15-0P 87362-17-2P 87362-18-3P 87362-19-4P  
 87362-20-7P 91511-91-0P 91511-92-1P  
 91511-93-2P 91511-94-3P 91511-95-4P 91511-96-5P  
 91511-97-6P 91511-98-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepn. and pharmacol. activity of)  
 IT 87362-09-2

RL: RCT (Reactant); RACT (Reactant or reagent)  
(condensation reaction of, with aldehydes)

RN 87362-09-2 HCAPLUS

CN Butanedioic acid, hydrazide 2-[(4-methylphenyl)sulfonyl]hydrazide (9CI)  
(CA INDEX NAME)



L48 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1984:209309 HCAPLUS

DN 100:209309

TI Some novel sulfanilyl derivatives

AU Cremllyn, R. J.; Swinbourne, F. J.; Batchelor, A.; Honeyman, R.; Nash, D.; Shode, O. O.; Patel, A.

CS Sch. Nat. Sci., Hatfield Polytech., Hatfield/Hertfordshire, UK

SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1983), 22B(10), 1029-43

CODEN: IJSBDB; ISSN: 0376-4699

DT Journal

LA English

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 5, 10

OS CASREACT 100:209309

AB Benzoic acid anilide and p-chloro, m-nitro, together with the 2,4-, 2,5- and 3,4-dichloro derivs., reacted with chlorosulfonic acid (I) in 1:4 molar ratios to give the corresponding sulfanilyl chlorides. However, nicotinic acid and isonicotinic acid anilides reacted with I, in 1:6 molar ratios only for conversion into the sulfanilyl chlorides. 2,4-Dichlorophenoxyacetic acid anilide reacted with I in 1:3 molar ratios to give the sulfanilyl chloride; this reaction when carried out in 1:7 molar ratios of the reactants gave the disulfonyl chloride. The various sulfanilyl chlorides were treated with amines, azide ion, and hydrazine to give a range of sulfonyl compds. The compds. prepd. have been subjected to preliminary biol. screening.

ST sulfanilyl prepn pharmacol antibacterial fungicide; benzanilide sulfanilyl

IT Bactericides, Disinfectants, and Antiseptics

Fungicides and Fungistats

(of sulfanilyl compds.)

IT 93-98-1 6043-39-6 6043-41-0 6043-42-1 6833-15-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(chlorosulfonylation of)

IT 89565-49-1P 89565-54-8P 89565-55-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and antibacterial activity of)

IT 89564-97-6P 89564-98-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and antiinflammatory activity of)

IT 89564-92-1P 89564-93-2P 89565-04-8P

RL: AGR (Agricultural use); BAC (Biological activity or effector, except

adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and fungicidal activity of)

IT 89564-87-4P **89565-05-9P**  
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and herbicidal activity of)

IT 89564-86-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and inhibition by, of cyclooxygenase thromboxane)

IT 89565-27-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction of, with diketones)

IT 67377-44-0P 89564-65-8P 89564-66-9P 89564-67-0P 89565-15-1P  
89565-24-2P 89565-43-5P 89565-65-1P 89565-66-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction of, with nitrogen contg. compds.)

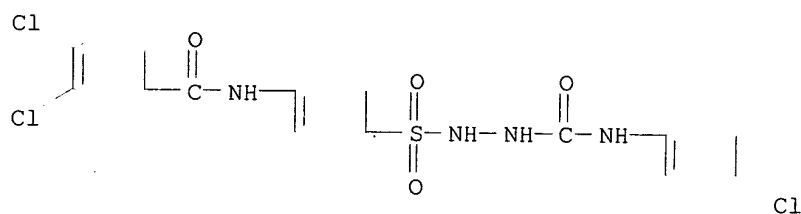
IT 89564-68-1P 89564-69-2P 89564-70-5P 89564-71-6P 89564-72-7P  
89564-73-8P 89564-74-9P 89564-75-0P 89564-76-1P 89564-77-2P  
89564-78-3P 89564-79-4P 89564-80-7P 89564-81-8P 89564-82-9P  
89564-83-0P 89564-84-1P 89564-85-2P 89564-88-5P 89564-89-6P  
89564-90-9P **89564-91-0P** 89564-94-3P 89564-95-4P  
89564-96-5P 89564-99-8P 89565-00-4P 89565-01-5P 89565-02-6P  
89565-03-7P 89565-06-0P 89565-07-1P 89565-08-2P 89565-09-3P  
89565-10-6P 89565-11-7P 89565-12-8P 89565-13-9P 89565-14-0P  
89565-16-2P 89565-17-3P 89565-18-4P 89565-19-5P 89565-20-8P  
89565-21-9P 89565-22-0P 89565-23-1P 89565-25-3P 89565-26-4P  
89565-28-6P 89565-29-7P 89565-30-0P 89565-31-1P 89565-32-2P  
89565-33-3P 89565-34-4P 89565-35-5P 89565-36-6P 89565-37-7P  
89565-38-8P 89565-39-9P 89565-40-2P 89565-41-3P 89565-42-4P  
89565-44-6P 89565-45-7P 89565-46-8P 89565-47-9P 89565-48-0P  
89565-50-4P 89565-51-5P 89565-52-6P 89565-53-7P 89565-56-0P  
89565-57-1P 89565-58-2P 89565-59-3P 89565-60-6P 89565-61-7P  
89565-62-8P 89565-63-9P 89565-64-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

IT 93-91-4 123-54-6, reactions 367-57-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with (isonicotinoyl)sulfanilylhydrazide)

IT 774-74-3  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with dimethylsulfonylamide)

IT **89565-05-9P**  
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and herbicidal activity of)

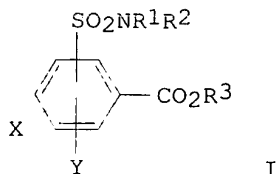
RN 89565-05-9 HCAPLUS  
CN Benzenesulfonic acid, 4-[(3,4-dichlorobenzoyl)amino]-,  
2-[[4-chlorophenyl)amino]carbonyl]hydrazide (9CI) (CA INDEX NAME)



L48 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1983:166900 HCAPLUS  
 DN 98:166900  
 TI Antiviral aminosulfonylhalobenzoic acids  
 IN Mochida, Ei; Suzuki, Yasuo; Yamaguchi, Kazuo; Ohnishi, Haruo  
 PA Mochida Pharmaceutical Co., Ltd., Japan  
 SO Eur. Pat. Appl., 35 pp.  
 CODEN: EPXXDW  
 DT **Patent**  
 LA English  
 IC A61K031-19; A61K031-235; A61K031-33  
 ICA C07C143-78; C07C143-72; C07D295-22  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1, 25, 27

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 68408	A1	19830105	EP 1982-105460	19820622
	R: BE, IT				
	JP 58000914	A2	19830106	JP 1981-96376	19810622
	JP 58192820	A2	19831110	JP 1982-75782	19820506
	SE 8203878	A	19821223	SE 1982-3878	19820622
	WO 8300013	A1	19830106	WO 1982-JP242	19820622
	W: CH, NL				
	AU 8285097	A1	19830106	AU 1982-85097	19820622
	AU 533742	B2	19831208		
	NL 8220205	A	19830502	NL 1982-20205	19820622
PRAI	EP 132540	A1	19850213	EP 1984-106186	19820622
	R: BE, IT				
	GB 2119651	A1	19831123	GB 1983-12121	19830504
	DE 3316611	A1	19831110	DE 1983-3316611	19830506
	FR 2526316	A1	19831110	FR 1983-7644	19830506
	JP 1981-96376		19810622		
	JP 1982-75782		19820506		
	EP 1982-105460		19820622		
	WO 1982-JP242		19820622		
GI					



I

AB Antiviral compns. (oral, nasal, rectal, parenteral, etc.), useful for the treatment of upper respiratory infection, pneumonia, bronchitis, etc.,



consist of aminosulfonyl(halo)benzoic acids (I, where X and Y = H, F, Cl, Br, NH, or NO<sub>2</sub>, R<sub>1</sub> = H or lower alkyl, R<sub>2</sub> = H, NH<sub>2</sub>, lower alkyl, hydroxyalkyl, alkoxy, aryl, guanyl, guanidino, ureido, oxamoylamino, or Cl-substituted pyridazinoamino groups or R<sub>1</sub> and R<sub>2</sub> together with N atom may form a satd. heterocycle, and R<sub>3</sub> = H, cyclohexyl, benzyl, aryl, or Cl-12 alkyl group; except not 3-aminosulfonyl-4-halobenzoic acid). I are prepd. by the reaction of a haloaminosulfonylbenzoyl chloride with an alc. or by the reaction of a chlorosulfonylbenzoic acid with an amine. Thus, a tablet contg. 200 mg 4-chloro-3-hydrazinosulfonylbenzoic acid [17749-21-2] was prepd. The antiviral activity of I against a variety of viral infections was demonstrated in mice.

ST aminosulfonylhalobenzoate virucide; halobenzoate aminosulfonyl virucide  
IT Virucides and Virustats

(aminosulfonyl(halo)benzoates)

IT 1429-44-3P 2295-63-8P 2736-23-4P 3086-91-7P 3585-45-3P  
4793-22-0P 4793-24-2P 4793-25-3P 4793-28-6P 5046-15-1P  
17749-21-2P 22892-96-2P 30170-05-9P 59210-61-6P 59210-63-8P  
59210-65-0P 59210-73-0P 62971-57-7P 83173-85-7P 83173-86-8P  
83173-87-9P 83173-88-0P 83173-89-1P 83173-90-4P 83173-91-5P  
83173-92-6P **83173-93-7P 83173-94-8P** 83173-95-9P  
83173-96-0P 83173-97-1P 85338-72-3P 85338-73-4P 85338-74-5P  
85338-75-6P 85338-76-7P 85338-77-8P 85338-78-9P 85338-79-0P  
85338-80-3P 85338-81-4P 85338-82-5P

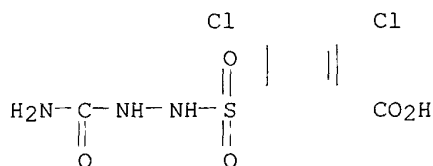
RL: THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(prepn. of, as virucide)

IT **83173-93-7P**

RL: THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(prepn. of, as virucide)

RN 83173-93-7 HCAPLUS

CN Benzoic acid, 5-[[2-(aminocarbonyl)hydrazino]sulfonyl]-2,4-dichloro- (9CI)  
(CA INDEX NAME)



L48 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1983:106925 HCAPLUS

DN 98:106925

TI Synthesis of sulfanilamido-naphthoquinones as potential antituberculous agents

AU Osman, S. A. A.; Abdalla, A. A.; Alaib, M. O.

CS Fac. Pharm., Univ. Khartoum, Khartoum, Sudan

SO Journal of Pharmaceutical Sciences (1983), 72(1), 68-71

CODEN: JPMSAE; ISSN: 0022-3549

DT Journal

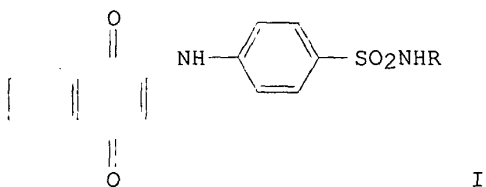
LA English

CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

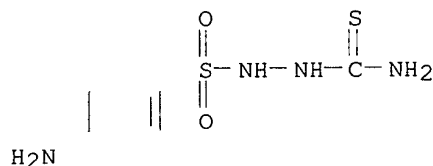
Section cross-reference(s): 1, 27

OS CASREACT 98:106925

GI

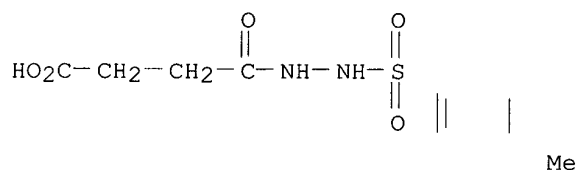


- AB 4-H2NC6H4CO2H, the acid hydrazides of PhCO2H, 2-HOC6H4CO2H, and isonicotinic acid, and (4-H2NC6H4)2SO2 condensed with 4-H2NC6H4SO2Cl to give N1-substituted sulfanilamides. These were then treated with 1,4-naphthoquinone to yield I (R = p-C6H4CO2H, NHBz, etc.). The partition coeff. for I showed, in some cases, high diffusion rates to the org. phase, benzene from physiol. Tyrode's soln. I are effective in low concn. in dioxane against the human sensitive strain of Mycobacterium tuberculosis. Sulfanilamides obtained from p-aminosalicylic acid and thiosemicarbazide failed to react with 1,4-naphthoquinone. These sulfanilamides also showed high activity against the same Mycobacterium.
- ST sulfanilamidonaphthoquinone prepn antitubercular; naphthoquinone sulfanilamido prepn antitubercular
- IT Tuberculostatics  
(sulfanilamide-naphthoquinone derivs.)
- IT 84907-40-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. and reaction of, with naphthoquinone)
- IT 6202-21-7P 6336-70-5P 84907-37-9P 84907-38-0P 84907-39-1P  
**84907-41-5P** 84907-42-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction of, with naphthoquinone)
- IT 84907-44-8P 84907-45-9P 84907-46-0P 84907-47-1P 84907-48-2P  
84907-49-3P 84907-50-6P 84907-51-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)
- IT 84907-43-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn., methylation, and ethylation of)
- IT 54-85-3 65-49-6 80-08-0 150-13-0 613-94-5 936-02-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with acetamidobenzenesulfonyl chloride)
- IT 130-15-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with sulfanilamides)
- IT 121-60-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reactions of, sulfonanilides from)
- IT **84907-41-5P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction of, with naphthoquinone)
- RN 84907-41-5 HCAPLUS
- CN Benzenesulfonic acid, 4-amino-, 2-(aminothioxomethyl)hydrazide (9CI) (CA INDEX NAME)



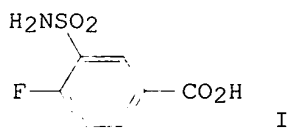
- L48 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1983:53299 HCAPLUS  
 DN 98:53299  
 TI Synthesis of arenesulfohydrazides of succinic acid and their methyl esters  
 AU Brizitskaya, A. N.; Gritsenko, I. S.; Salo, I. D.  
 CS Khark. Derzh. Farm. Inst., Kharkov, USSR  
 SO Farmatsevtichnii Zhurnal (Kiev) (1982), (5), 65-6  
 CODEN: FRZKAP; ISSN: 0367-3057  
 DT Journal  
 LA Ukrainian  
 CC 25-13 (**Benzenes**, Its Derivatives, and Condensed **Benzenoid** Compounds)  
 Section cross-reference(s): 1  
 AB Acylating RC<sub>6</sub>H<sub>4</sub>ZSO<sub>2</sub>NHNNH<sub>2</sub> (R = p-MeO, p-Me, p-Cl, p-Br, p-MeO<sub>2</sub>CNH, o-O<sub>2</sub>N, Z = bond; R = H, Z = CH<sub>2</sub>) with succinic anhydride in C<sub>6</sub>H<sub>6</sub> and/or with MeO<sub>2</sub>CCH<sub>2</sub>CH<sub>2</sub>COCl in abs. MeOH gave 10 corresponding RC<sub>6</sub>H<sub>4</sub>ZSO<sub>2</sub>NHNNHCOCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>R<sub>1</sub> (I; R<sub>1</sub> = H, Me, resp.) in 27-91% yield. I (R = R<sub>1</sub> = Me, Z = bond) was saponified to give the acid, and the latter esterified with abs. MeOH. I had hypoglycemic activity similar to that of butamide, and several I (R<sub>1</sub> = Me, Z = bond) had fungicidal and/or fungistatic activity.  
 ST sulfonhydrazide succinic prepn hypoglycemic fungistat;  
 arenesulfonhydrazide acylation; hydrazide arenesulfonic acylation  
 IT Acylation  
 (of arenesulfonhydrazides with succinic anhydride and Me succinoyl chloride)  
 IT Antidiabetics and Hypoglycemics  
 Fungicides and Fungistats  
 (succinic arenesulfonhydrazides)  
 IT Sulfonamides  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (succinic arenesulfonhydrazides, prepn. and hypoglycemic and fungistatic activity of)  
 IT 108-30-5, reactions 1490-25-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of arenesulfonhydrazides with)  
 IT 1879-26-1 5906-99-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of, with Me succinoyl chloride)  
 IT 1576-35-8 2297-64-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of, with succinic anhydride)  
 IT 1950-68-1 2751-25-9 36331-57-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of, with succinic anhydride and with Me succinoyl chloride)  
 IT **84290-89-1P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and esterification of)  
 IT **84290-94-8P 84290-96-0P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and hypoglycemic and fungistatic activity of)

IT 84290-90-4P 84290-91-5P **84290-92-6P** 84290-93-7P  
**84290-95-9P** 84290-97-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT 84315-49-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn., sapon. and hypoglycemic and fungistatic activity of)  
 IT **84290-89-1P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. and esterification of)  
 RN 84290-89-1 HCAPLUS  
 CN Butanedioic acid, mono[2-[(4-methylphenyl)sulfonyl]hydrazide] (9CI) (CA  
 INDEX NAME)



L48 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2003 ACS  
 AN **1982:550747** HCAPLUS  
 DN **97:150747**  
 TI Antiviral compositions containing aminosulfonylhalobenzoic acid  
 derivatives  
 IN Mochida, Ei; Suzuki, Yasuo; Yamaguchi, Kazuo; Ohnishi, Haruo  
 PA Mochida Pharmaceutical Co., Ltd., Japan  
 SO Fr. Demande, 23 pp.  
 CODEN: FRXXBL  
 DT **Patent**  
 LA French  
 IC A61K031-19  
 ICA C07C143-78  
 CC 63-6 (**Pharmaceuticals**)  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2493702	A1	19820514	FR 1981-21017	19811110
	FR 2493702	B1	19841012		
	JP 57081411	A2	19820521	JP 1980-157971	19801110
	JP 58017167	B4	19830405		
	JP 58000914	A2	19830106	JP 1981-96376	19810622
PRAI	NL 8220205	A	19830502	NL 1982-20205	19820622
	JP 1980-157971		19801110		
PRAI	JP 1981-96376		19810622		
	JP 1982-75782		19820506		
	WO 1982-JP242		19820622		
GI					



AB Oral, parenteral and nose drop formulations of 31 aminosulfonylhalobenzoic acid derivs., e.g., 3-aminosulfonyl-4-fluorobenzoic acid (I) [1535-45-1], were prep'd. for the treatment of viral infections, esp., those of the upper respiratory tract. The antiviral activity of these compds. against influenza (A0, A2), parainfluenza type 3, ECHO, etc., viruses is reported.

ST aminosulfonylhalobenzoate virucide; sulfonylaminohalobenzoate virucide; benzoate aminosulfonylhalo virucide

IT Virucides and Virustats  
(aminosulfonylhalobenzoic acid derivs.)

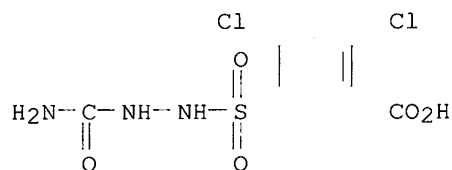
IT Respiratory tract  
(disease, viral infection, aminosulfonylhalobenzoic acid derivs. for treatment of)

IT 1205-30-7P 1429-44-3P 1535-45-1P 2295-63-8P 2736-23-4P  
3086-91-7P 3585-45-3P 4793-22-0P 4793-24-2P 17749-21-2P  
22892-96-2P 59210-61-6P 59210-63-8P 59210-65-0P 59210-73-0P  
59815-19-9P 62971-57-7P 82608-96-6P 83173-85-7P 83173-86-8P  
83173-87-9P 83173-88-0P 83173-89-1P 83173-90-4P 83173-91-5P  
83173-92-6P **83173-93-7P** **83173-94-8P** 83173-95-9P  
83173-96-0P 83173-97-1P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and antiviral activity of)

IT **83173-93-7P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and antiviral activity of)

RN 83173-93-7 HCAPLUS

CN Benzoic acid, 5-[[2-(aminocarbonyl)hydrazino]sulfonyl]-2,4-dichloro- (9CI)  
(CA INDEX NAME)



L48 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1968:475378 HCAPLUS

DN 69:75378

TI Derivatives of 5-phenyl-2,4-pentadienoic acid as potential antimalarial agents

AU Werbel, Leslie M.; Headen, Nancy; Elslager, Edward F.

CS Res. Lab., Parke, Davis and Co., Ann Arbor, MI, USA

SO Journal of Medicinal Chemistry (1968), 11(5), 1073-4  
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

CC 15 (Pharmacodynamics)

GI For diagram(s), see printed CA Issue.

AB I [where X and Y are H or Cl; and R = NHCSNH<sub>2</sub>, NMe(OMe), CH<sub>2</sub>CH<sub>2</sub>NEt<sub>2</sub>, N(CH<sub>2</sub>CO<sub>2</sub>Et)COCH:CHCH:CHPh, N(CH<sub>2</sub>CH<sub>2</sub>NEt<sub>2</sub>)COCH:CHCH:CHPh, NHCOMe, NHCO<sub>2</sub>Et, NHSO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Me-p, N(CH<sub>2</sub>CH<sub>2</sub>OH)COCH:CHCH:C<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>, (CH<sub>2</sub>)<sub>3</sub>NHCOCH:CHCH:CHC<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>, or iso-Pr; or R = iso-Pr, Y = H, and X = Me, Br, or Ph] were inactive against Plasmodium bergeri and P. gallinaceum. I (R = iso-Pr, Y = H, X = Cl) had previously been reported to be active against P. gallinaceum.

ST **antimalarial** agents; Plasmodium inhibitors; inhibition  
Plasmodium

IT **Malaria**  
(**antimalarial** substances, 5-phenyl-2,4-pentadienoic acid  
derivs. in relation to)

IT 18887-92-8P 18887-93-9P **18887-94-0P** 18887-95-1P  
21480-12-6P 21480-13-7P 21480-15-9P 21480-16-0P 21480-17-1P  
21480-19-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic  
use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and **antimalarial** activity of)

IT **18887-94-0P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic  
use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and **antimalarial** activity of)

RN 18887-94-0 HCAPLUS

CN 2,4-Pentadienoic acid, 5-(3,4-dichlorophenyl)-, 2-[(4-  
methylphenyl)sulfonyl]hydrazide (9CI) (CA INDEX NAME)

